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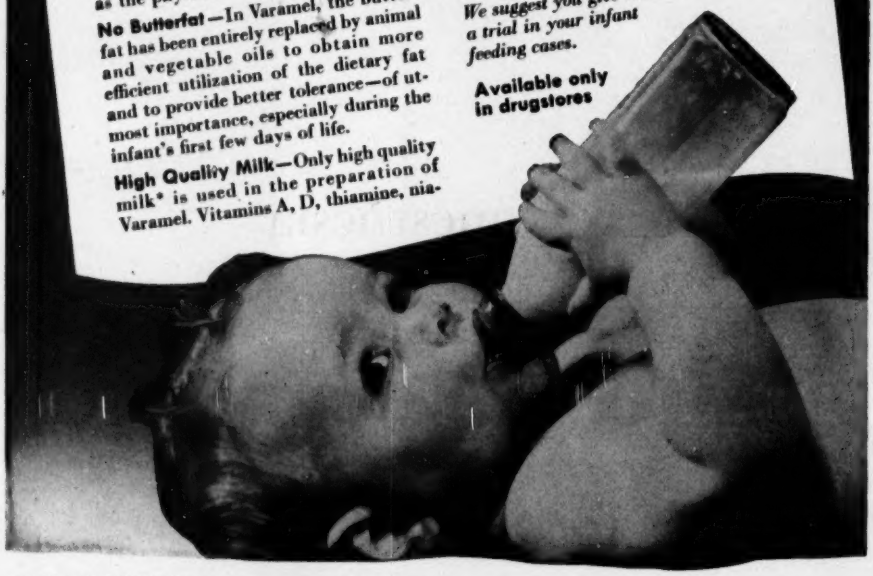

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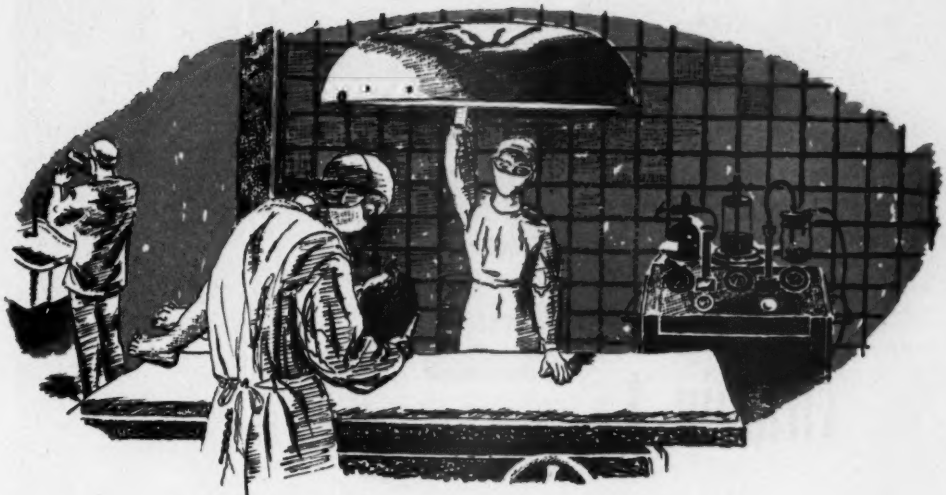

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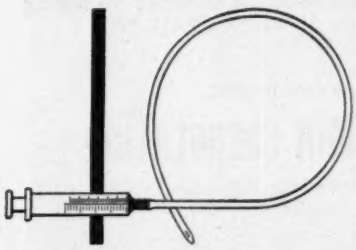

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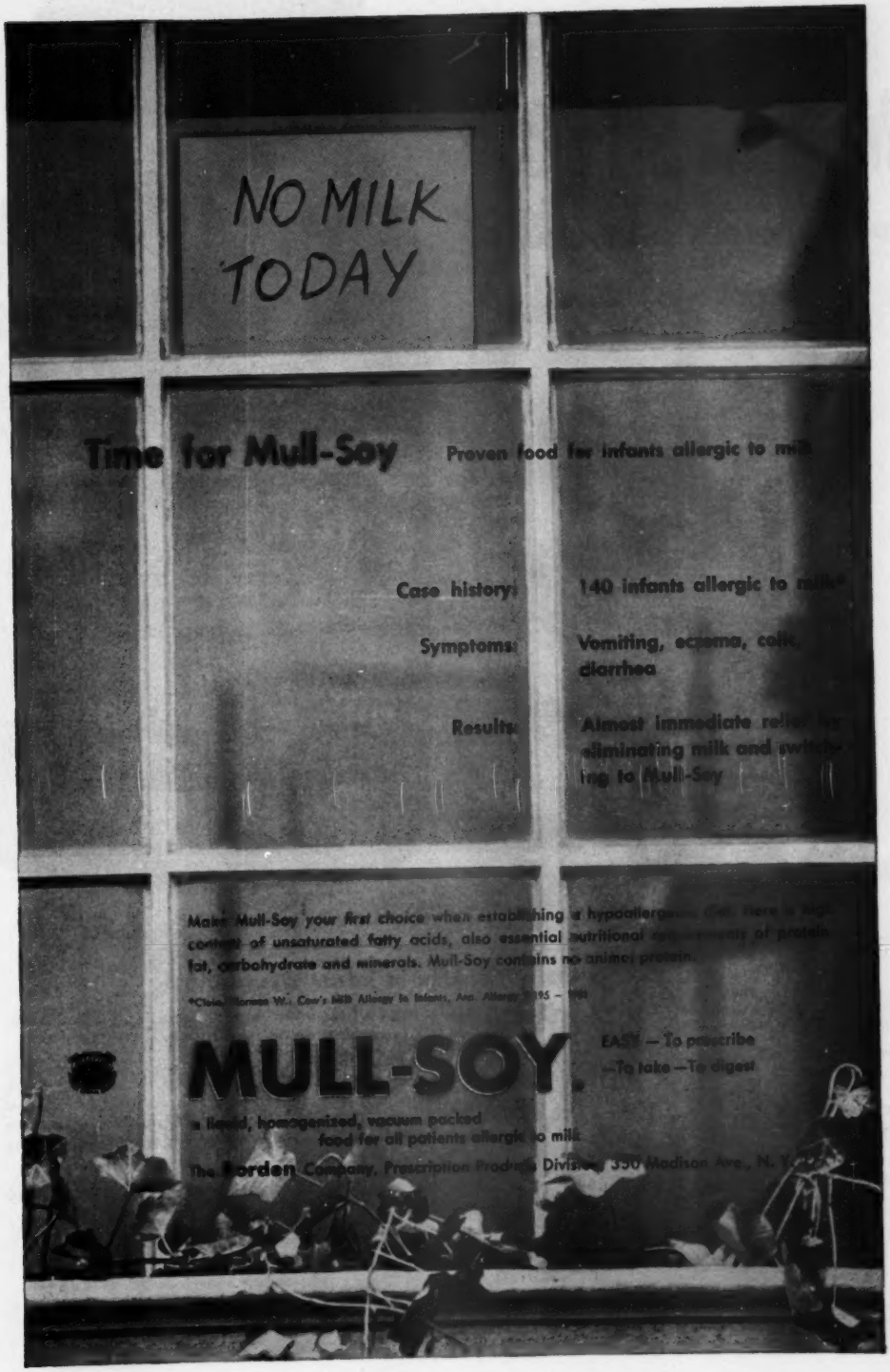
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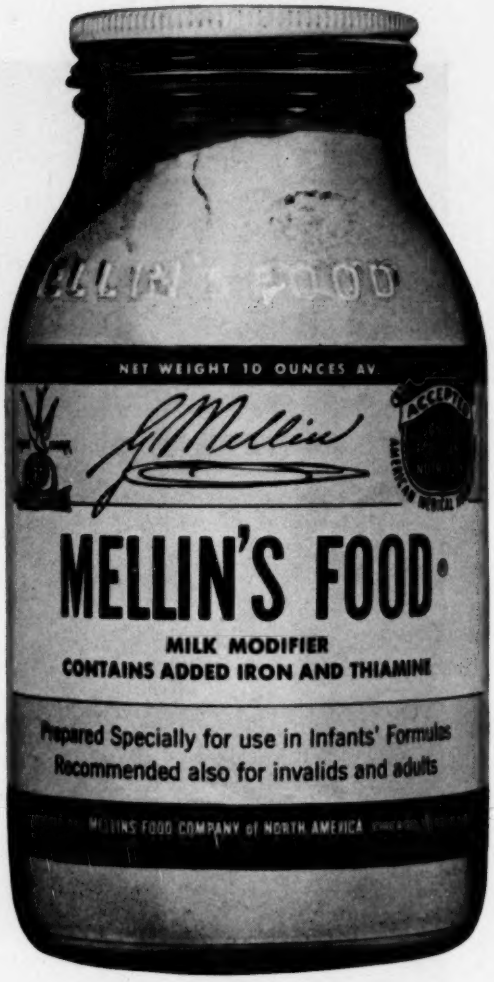
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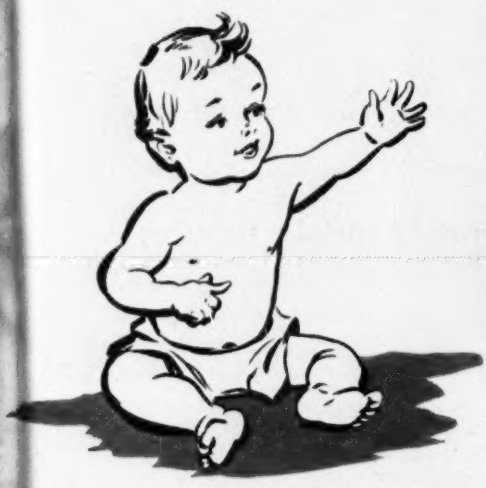

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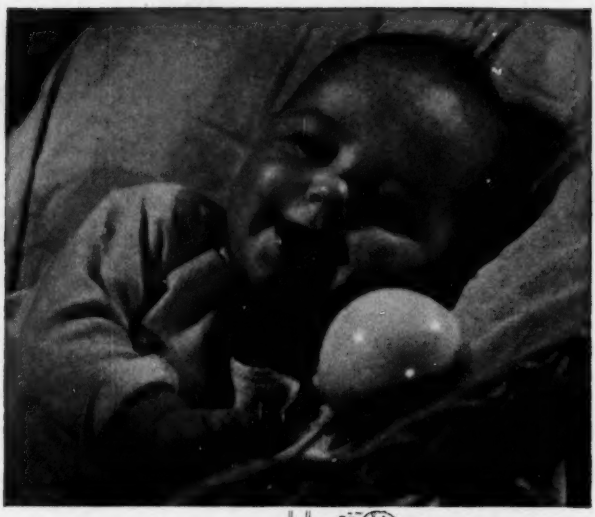

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A. M. A.
American Journal of Diseases of Children

VOLUME 84 JULY 1952 NUMBER 1

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SOME IDEAS ON THE NATURE OF RHEUMATIC FEVER

Presidential Address

HUGH McCULLOCH, M.D.
CHICAGO

THE HONOR and distinction conferred by this Society in making one of its members its President each year places a heavy responsibility on that member. Appreciation alone would make one humble. When one reflects on those members who, in the past, have occupied this position, humility becomes a dominant feeling in assuming that responsibility, for the Society does represent pediatrics in this country both through the sixty and more years of its existence and at the present time. I am deeply grateful to you.

The story of rheumatic fever in the past sixty-five years as reflected in the records of the Society has been one of insignificant importance. Programs have contained papers from time to time on the subject, and many of its members have had a known interest in solving some of the problems. The quantity of presentation on the programs may have been no more than a reflection of what has taken place in this time with respect to new developments in studies of rheumatic fever. And a careful review of this period elsewhere indicates a dearth of new information concerning the disease.

This Society was founded and crystallized into being at the same time that Cheadle clarified many important ideas of rheumatic fever and rheumatic heart disease in children. Much of what he pointed out has remained the best concept of the disease to this time. His classic descriptions remain clear. Very little has been added in this sixty-five years that is accepted or that has modified his description.

My own sixty odd years have been spent in this same area of interest, and now for forty of those years, since 1913, this interest has been a dominant one. For in that year a small boy with advancing rheumatic heart disease was under my care through almost his entire illness including his death and postmortem examination. I still have a deep yearning to know why rheumatic fever developed in this child, why we could do nothing to arrest the progress of the disease, and why his heart should have looked as it did. During these years much time and effort have been spent in "brooding" over these questions and the problems involved in working out the answers. The dearth of new facts and the failure to learn more concerning rheumatic fever are due to no lack of action or effort in investigation, and today these efforts continue with great zeal and earnestness by many workers in many fields.

Chief-of-Staff and Director, Medical Service, La Rabida Jackson Park Sanitarium.

Read at the Sixty-Second Annual Meeting of the American Pediatric Society, Old Point Comfort, Va., May 7, 1952.

"Brooding" does not imply lack of action. It is a state of mind in which there is freedom of thought and the opportunity to search abstractly for ideas that may open the way to a better understanding.

Rheumatic fever continues to be an important health problem for young people. A statistical evaluation of its extent since the beginning of this century, however reliable such vital statistics may be, indicates a gradual but constant downward trend in its morbidity and mortality rates. No observable factor has surely contributed to this downward trend though several are probable: a better understanding of the disease, the effect of public health and preventive medical procedures, and the introduction of control measures for streptococcal infection. But most of Cheadle's concept remains true, and answers have yet to be found for the big questions not included in his concept.

Rheumatic fever is a disease of young people, and its course must be a part of those processes and changes which represent evolutionary and progressive growth. The residual heart disease, the end result of the injury and, in its residual form, the scar of that injury, healed and arrested, may be found at all ages. And at times even in later years the healing of the injury may be still present. But why does the rheumatic state develop in young people? And why are certain young people selected and not all young people? What factors in the several components of growth are responsible for the setting of the stage for the attack of rheumatic fever? What are the alterations of the growth pattern? The important changes in growth at six years of age, the end of a stable growth period of preschool life, and the emergence of a new pattern of growth can profoundly influence the child. This is the age when first attacks of rheumatic fever occur most frequently. These changes have received less attention and are not so well understood as those that occur at 12 years of age, and even this period is not yet understood. The latter period is also one of emergence of a new pattern of growth and a time when the course of rheumatic fever is modified or the pattern of the disease may change greatly. Are the changes related to deficiency, to normal or abnormal quantitative retardation and acceleration, or to a qualitative deviation from the standard pattern of growth? And is the standard pattern altered by a primary intrinsic factor or by a secondary factor such as nutrition or infection and others? Recent studies on the effect of growth hormones on rheumatic disease have been interesting and open the way to further investigation of the relationship of growth and rheumatic fever. The answer to some of our problems may come from this source.

Rheumatic fever is closely related to nutritional deficiency or failure, and careful metabolic studies would indicate the existence of such deficiency before the onset of the initial attack. Clinical examination reveals common signs of malnutrition in most patients, and continued studies of patients after the attack reveal in large degree the nature and extent of the deficiency. The interrelationship of nutritional deficiency and the alteration of the growth pattern is close. A review of the record preceding the attack of rheumatic fever reveals that the nutritional deficiency was preexisting and primary, whatever the effect of an attack may be subsequently on the nutritional state. The nature of the nutritional deficiency is not clear, but evidence suggests that it is in that of protein intake and those proteins particularly concerned with the formation and metabolism of collagen tissue. Food diaries of patients always reveal distressing inadequacies of foods known to be valuable in

maintaining superior nutritional levels and usually insufficient to maintain even minimal levels. But other children, even in the same family, with similar dietary inadequacies do not have rheumatic fever. The ability of an individual to convert food stuffs into collagen tissue may determine the difference. We are now looking to the chemist to learn the mechanism of this conversion process.

Rheumatic fever in its natural course and behavior presents itself as an attack or some other form of clinical activity when the patient becomes ill. Why does the person become ill, and was he a patient with rheumatic disease before he became clinically ill or did he spontaneously acquire a new state? The natural course of rheumatic fever suggests that he was a patient previously in a state vulnerable to a convergence of events and circumstances which bring on an attack. Attacks of rheumatic fever are usually related to the presence of an active streptococcal infection and in the opinion of many workers even specifically to a Group A beta hemolytic Streptococcus. But patients do not always reveal the presence of an active streptococcal infection. In those who do show streptococcal infection there is no evidence that the organisms have appeared at the site of the tissue change and no acceptable evidence that the tissue changes always represent a response to the organism or to any of its products. Can it be that the streptococcal infection, therefore, represents a phenomenon of stress operating to disturb the balance of the individual poorly prepared to receive the stress and whose ability to respond is inadequate? Attacks are known to have developed in rheumatic subjects from other forms of stress, such as extreme fatigue, exposure to unusual physical agents of heat or cold, and emotional disturbances. It may be that it is the factor of stress rather than the specific nature of the stress that determines the onset of the attack. Recent studies of adrenal gland physiology and body function suggest some of the mechanisms by which rheumatic fever may develop in the vulnerable individual. Of particular interest is the suggested relationship between adrenal function and that of the pituitary gland and supposedly hormones from that gland related to the growth process. "Brooding" on this phase of the nature of rheumatic fever becomes excitingly hopeful of real action. The endocrine and enzyme chemist with new technics may clear the way. I have searched again through Cheadle's report for any sign that he had this concept in mind. This seems to be outside of his thinking, for neither he nor any others of his day knew much of the basic facts of adrenal or pituitary function. But he did know that rheumatic fever had a peculiar expression as a disease of young people and was therefore related to the growth process.

Rheumatic fever is a disease distributed throughout the body and affecting collagen tissue and maybe other tissue cells in most of the vital organs. But the heart seems to be most frequently and most severely affected. It was in the patient whom I saw in 1913. Also when recovery from the injury sets in, the process is reversible and complete in all tissues and organs save the heart. The injury in the heart too is usually reversible, but why does it happen that in a reasonably large proportion of patients the repair results in a scar with destruction of vital elastic and muscle cell tissue? And why is it true that long after all clinical signs of injury and repair have reversed themselves and disappeared there is a lingering smoldering active process in cardiac muscle tissue? This active process lies far below the threshold of ordinary clinical recognition, and there is a real challenge to the over-all

programs of care for rheumatic subjects. Heart disease therefore is the measure of rheumatic fever and must be used to indicate the progress of the patient, his recovery, and the success of that program. Publication of figures on follow-up studies of patients over a period of twenty years after discharge from The House of The Good Samaritan includes a significantly large group of patients in whom signs of heart disease developed long after their discharge. Can this be prevented if adequate recognition, treatment, and subsequent care are obtained with sufficient frequency and accuracy to warrant patients carrying out the measures proposed to this end? Studies at La Rabida Sanitarium indicate presently that rheumatic heart disease in an active stage can be modified in important ways by therapeutic use of selected hormonal agents from the pituitary gland. These studies have not indicated the mechanisms by which this comes about, and the question remains to be solved. But some mechanism is present, and the effect can be obtained. Can this effect be obtained in other patients and with a better understanding of the mechanism, can the smoldering lingering carditis be controlled and arrested? The answer to that question will be yes.

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PROTEIN-BOUND IODINE LEVELS IN NORMAL AND IN DIABETIC CHILDREN

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THE DEVELOPMENT of reliable semimicroanalytic procedures has permitted more precise studies of the circulating iodine fractions.[1] As a consequence, much of the confusion resulting from methodologic inadequacies and from the use of blood instead of serum samples has been eliminated. In brief, applications of these methods have revealed that the level of serum inorganic iodide in healthy adults varies, as might be expected, with the intake of this halide, but with an ordinary diet it only infrequently exceeds 1 γ per 100 ml.[2] The major fraction, called protein-bound or serum-precipitable iodine, ranges in euthyroid adults between 4 and 8 γ per 100 ml.,[3] remains quite constant in any one person from week to week,[4] and from the point of view of solubility, behaves like thyroxine.[5] Thyro-

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3. Winkler, A. W., in Duncan, G. G.: Diseases of Metabolism, Ed. 2, Philadelphia, W. B. Saunders Company, 1947, pp. 896-938.

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toxicosis [6] and uncomplicated pregnancy [7] are characterized by elevations of both protein-bound iodine and of thyroxine.[8] Hypothyroidism, or myxedema,[9] and some but not all instances of hypoproteinemia [10] are associated with decreased concentrations of these iodine fractions. It has also been recognized that organic dyes interfere with identification of the endogenous moieties [11] and that sufficiently prolonged therapy with inorganic iodides will raise the nonthyroxine portion of the protein-bound iodine.[12]

These various studies have permitted quite precise evaluation of thyroid function in adults. Comparable data on younger subjects have been either limited or entirely absent. The recent completion of measurements of protein-bound iodine and of thyroxine in 110 unselected healthy infants [13] has emphasized the need for studies in the other age groups. It is clear, for example, that at birth and for weeks or months later criteria based on adult values are not at all applicable. The observations herein reported fill some of the gaps still present despite earlier informative reports from other laboratories.[14]

MATERIALS AND METHOD

Sera have been obtained from the entire population, 64 in number, of a well-conducted home for children [15] 6 to 18 years old. The subjects were well nourished and healthy. Most of them were of North European stock. Everyone attended school in a grade appropriate to his or her chronologic age. For purposes of comparison a similar number of children with diabetes mellitus were selected at random from the outpatient department and the diabetic ward of Children's Hospital. In all of these, the diabetic state was under satisfactory control with dietary restriction and insulin administration, as indicated by the state of nutrition, urine volumes, and degree of glycosuria.

The analytic method employed in each group of subjects for measurement of protein-bound iodine has been described in detail in a previous publication.[12b] It is modified slightly from that

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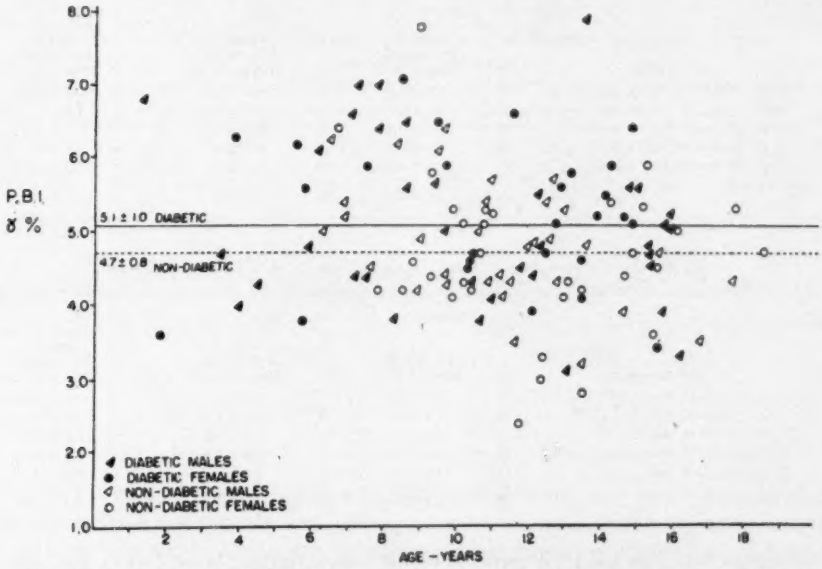
15. The cooperation of the Board and the personnel of the Protestant Home for Children is acknowledged.

published by Barker [16] and in our hands has yielded experimental errors of a fraction of a microgram. In addition sera have been analyzed for protein content either by the macromethod of Kjeldahl [16] or estimated by gravimetry.[17] The protein values all fell within the normal range.[17]

In both groups of subjects concentrations of protein-bound iodine have been related to sex and to age, and in the nondiabetic children to growth and mental development as well. With respect to the latter, physical growth has been evaluated by measurements of height and weight of each child and interpreted by reference to tables presented by Stuart and Stevenson.[18] These two measurements constitute an adequate index for purposes of this paper, although their limitations must be borne in mind. Intellectual competence of 40 of the normal children was evaluated by means of the Stanford-Binet test and is expressed here by intelligence quotients. Similar comparisons have not been made in the diabetic group.

RESULTS

The distribution of values for protein-bound iodine in the serum in these two groups of subjects is shown in the accompanying chart. The 3d-to-97th percentile



Values for protein-bound iodine in the serum, plotted against the age of the subjects. The dotted horizontal line at 4.7 γ per 100 ml. represents the mean value for the nondiabetic children; the solid line at 5.1 refers to the diabetic patients. There is no statistically significant difference between these two means, but the older children appear to have somewhat lower concentrations of iodine.

16. Majoor, C. L. H.: The Possibility of Detecting Individual Proteins in Blood Serum by Differentiation of Solubility Curves in Concentrated Sodium Sulfate Solutions: II. Comparison of Solubility Curves with Results of Electrophoresis Experiments, J. Biol. Chem. **169**:583-594 (Aug.) 1947. Milne, J.: Serum Protein Fractionation: A Comparison of Sodium Sulfate Precipitation and Electrophoresis, ibid. **169**:595-599 (Aug.) 1947.

17. Danowski, T. S., and Gilmore, G. H.: Relationships Between Serum Water or Weight and Protein Concentration, J. Lab. & Clin. Med. **35**:67-75 (Jan.) 1950.

18. Stuart, H. C., and Stevenson, S. S.: Care and Evaluation of Well Children: Physical Growth and Development, in Mitchell-Nelson's Textbook of Pediatrics, edited by W. E. Nelson, Ed. 5, Philadelphia, W. B. Saunders Company, 1950, pp. 14-59.

limits extend from 3.2 to 7.0 γ whereas concentrations between 4.0 and 6.0 γ make up the 20th-to-80th percentile range. There is no statistically significant difference between the mean value for the diabetic children and that obtained for the nondiabetic controls. The distribution of the individual points suggests that with increasing age somewhat lower levels of protein-bound iodine are encountered. Tables 1 and 2 therefore present findings according to age and sex. Tables 3 and 4 are based on comparisons of mean iodine values with weight, height, and intelligence quotient of normal children.

The value for protein-bound iodine recorded in the group of nondiabetic children aged 12 years 10 months to 14 years 9 months (Table 1) is statistically significantly lower than those observed in either of the two preceding age categories

TABLE 1.—*Protein-Bound Iodine Concentrations of Normal Boys and Girls of Various Ages*

	Children		Boys		Girls	
Age Group	No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.
6 yr. 3 mo.-9 yr. 4 mo.....	15	5.3 ± 1.1	8	5.2 ± 0.8	7	5.3 ± 1.4
9 yr. 6 mo.-10 yr. 11 mo.....	15	4.9 ± 0.7	7	5.1 ± 0.9	8	4.8 ± 0.5
11 yr. 0 mo.-12 yr. 8 mo.....	14	4.4 ± 1.0	10	4.8 ± 0.7	4	3.5 ± 1.2
12 yr. 10 mo.-14 yr. 9 mo.....	10	4.1 ± 0.7	4	4.0 ± 0.7	6	4.2 ± 0.8
14 yr. 11 mo.-18 yr. 7 mo.....	10	4.7 ± 0.8	3	4.2 ± 0.6	7	4.9 ± 0.7
	64	4.7 ± 0.8	32	4.8 ± 0.8	32	4.6 ± 0.8

TABLE 2.—*Protein-Bound Iodine Concentrations in Diabetic Children*

	Children		Boys		Girls	
Age Group	No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.
1 yr.-6 yr. 11 mo.....	11	5.1 ± 1.2	6	5.1 ± 1.1	5	5.1 ± 1.5
7 yr.- 9 yr. 11 mo.....	15	5.8 ± 1.0	11	5.7 ± 1.1	4	6.4 ± 0.6
10 yr.-12 yr. 11 mo.....	14	4.6 ± 0.5	7	4.5 ± 0.5	8	5.0 ± 0.8
13 yr.-14 yr. 11 mo.....	11	5.3 ± 0.6	4	5.5 ± 2.0	9	5.3 ± 0.7
15 yr.-16 yr. 11 mo.....	11	4.6 ± 0.7	10	4.7 ± 0.7	1	3.4
	64	5.1 ± 1.0	37	5.0 ± 1.0	27	5.3 ± 1.0

(p values, 0.035 or less). A trend to higher concentrations is evident in the group which follows. Similar comparison following separation by sex suggests that in the boys the lowest recorded mean values for protein-bound iodine are found in the group aged 12 years 1 month to 14 years 9 months, whereas in girls the minimal value appears earlier, i. e., in the group aged 11 years to 12 years 1 month. The total number of observations, however, is small.

The mean protein-bound iodine of diabetic children in the age range from 10 years to 12 years 11 months (Table 2) is lower than that characteristic of the groups which immediately precede and follow it (p, 0.0007 and 0.007, respectively). It is also lower than that obtained by combining the remaining age groups. It should be pointed out that even though the distribution as to age is not comparable, this trend is similar to that observed in the normal children. The low values for protein-bound iodine in the group aged 15 years to 16 years 11 months are commented upon in later discussion.

Table 3 shows concentrations of protein-bound iodine of normal children, selected from the group of 64 because their weight and height measurements fall in the 90th percentile category or above and the 10th percentile category or below. The concentrations show no significant variations from each other or from the mean concentration for the entire group.

Table 4 presents concentrations of protein-bound iodine of children selected because their intelligence quotients are below 90 or above 110. The lowest intelligence quotient represented is 73, and the highest is 124. The duller children show a lower mean concentration of protein-bound iodine in the serum, and the two means vary significantly from each other (p, 0.04), but the number of observations is small.

COMMENT

Evidence has been cited earlier that in adult subjects the serum concentration of protein-bound iodine is a useful and delicate measure of thyroid activity. In children

TABLE 3.—*Protein-Bound Iodine Concentrations of Normal Children in Various Percentile Categories*

Weight in 90th Percentile or Above		Weight in 10th Percentile or Below		Height in 90th Percentile or Above		Height in 10th Percentile or Below	
No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.
7	5.0 ± 1.6	8	4.4 ± 0.6	10	4.7 ± 0.7	5	5.1 ± 1.2

TABLE 4.—*Protein-Bound Iodine Concentrations of Normal Children in Two Intelligence-Quotient Categories*

I. Q. Below 90		I. Q. Above 110	
No.	PBI γ Per 100 Ml., Mean ± S. D.	No.	PBI γ Per 100 Ml., Mean ± S. D.
9	4.4 ± 0.9	8	5.2 ± 0.5

as well as in adults determinations of basal metabolic rate and serum concentration of cholesterol are variable and have not proved entirely satisfactory as indices of thyroid function.[19] Evaluation of osseous development in children is of limited value as an index, since bone age may be markedly affected by disease and malnutrition and, at best, exhibits considerable variation. Hence, the serum levels of protein-bound iodine obtained from a series of healthy children and presented here should facilitate the diagnosis of thyroid malfunction.

The trend toward lower concentrations in early adolescence in the nondiabetic as well as in the diabetic childen is not consistent with the generally held concept of a physiologic prepubertal hyperthyroidism. This finding is in keeping with the views expressed by Shock.[20]

19 Means, J. H.: The Thyroid and Its Diseases, Ed. 2, Philadelphia, J. B. Lippincott Company, 1948.

20. Shock, N. W.: Physiological Changes in Adolescence, in Adolescence, Forty-Third Yearbook, National Society for the Study of Education: Pt. I. Chicago, University of Chicago Press, 1944, pp. 56-79.

These norms show no correlation of protein-bound iodine levels with body weight or height in nondiabetic healthy children. The significant correlation with cerebration as measured by intelligence quotients, i. e., children of lower intelligence had lower levels of protein-bound iodine, may be merely a further indication of a generally inadequate development and does not, of course, establish a cause-effect relationship. On the other hand, the limited number of observations on this point has already been emphasized.

The occurrence of low values of protein-bound iodine in the oldest diabetic children included in this study may be related to the relatively greater severity of the diabetic state in this age group,[21] resulting in discharge of adrenal cortex steroids secondary to ketosis or to hypoglycemia.[22] It is known that adrenal steroids can produce a profound lowering of protein-bound iodine in the serum.[23]

SUMMARY AND CONCLUSIONS

Since serum concentration of protein-bound iodine is a reliable measure of thyroid function in adults, standards have been obtained based on 64 apparently normal children, aged 6 through 18 years. The level averaged 4.7 $\pm$ 0.8 γ per 100 ml. This mean value was not influenced by sex or by normal variations in physique.

In a comparable number of children under treatment for diabetes mellitus the mean value for protein-bound iodine was found to be statistically indistinguishable, 5.1 $\pm$ 1.0 γ per 100 ml.

A trend toward lower levels was evident in the early adolescent years in nondiabetic as well as in diabetic children.

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EARLY IMMUNIZATION—ITS POSSIBLE INFLUENCE ON CANADIAN MORTALITY FIGURES

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RECENTLY there has been a trend toward starting inoculations against diphtheria and whooping cough at an age earlier than 6 to 7 months. In reply to a questionnaire which was answered by 9 of 12 Medical Officers of Health of various cities in Canada, 6 indicated that they were recommending immunization against these two diseases starting at 3 to 4 months of age. Neither Montreal nor Toronto, Canada's two largest cities, endorse this view at the moment.

One of the principal objectives of any immunization program is the reduction of mortality. Before any change in a program should be considered therefore, one must ask at least two questions. First of all, is the program that is now in use satisfactory? That is, is there really any necessity for changing it? Second, will the recommended change make any difference in mortality figures?

TABLE 1.—*Number of Diphtheria Deaths in Canada, 1939-1948*

1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	Total
336	218	240	256	287	309	271	227	140	86	2,365

Table 1 shows the total number of deaths from diphtheria which occurred in all Canada for the 10 years 1939-1948, inclusive.[1] No information is available as to which of these deaths occurred among the inoculated and which occurred among those who had received no immunization. It is merely the residuum after the various immunization programs throughout Canada have been carried out.

So far as diphtheria is concerned, over a period of 10 years 2,365 deaths occurred. When one analyzes this, it is evident that until 1947 the number of deaths ran well over 200 a year, whereas in 1947 and 1948 a sharp drop occurred. This drop is significant statistically.[2]

Deaths from whooping cough over the same 10-year period totaled 4,001.[1] Until 1946 these averaged between 400 and 500 a year, but in 1946 a drop occurred and by 1948 a low level of 155 was reached. Again, this is of statistical significance.[2]

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1. Vital Statistics Section, Dominion Bureau of Statistics, Ottawa, Ont., Canada. Personal communication to the author.

2. Migicovsky, B. B.: Personal communication to the author.

It is interesting to note that these reductions in the number of deaths occurred before Canadian health departments changed to earlier immunization and, indeed, occurred before most of the papers urging this change were published. It is therefore apparent that, whether due to an inoculation program or to other factors, a drop in the Canadian mortality figures for diphtheria and whooping cough was actually occurring with the older programs. Furthermore, this drop was concurrent with a similar drop in reported morbidity rates,[1] as shown in Table 3. It would

TABLE 2.—*Number of Whooping Cough Deaths in Canada 1939-1948*

1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	Total
541	628	437	560	416	337	470	231	232	155	4,001

TABLE 3.—*Morbidity Case Rate per 100,000 Population*

1939	1940	1941	1942	1943	1944	1945	1946	1947	1948
				Diphtheria					
25.8	20.5	24.9	25.4	23.8	27.0	23.0	20.6	12.3	7.0
				Whooping Cough					
159.8	174.9	144.9	158.0	161.8	103.6	100.7	62.5	82.2	55.1

TABLE 4.—*Deaths in Canada 1939-1948 Inclusive*

Age, Yr.	Diphtheria	Per Cent	Cumulative Per Cent
0- 1	211	8.9	8.9
1- 2	178	7.5	16.4
2- 3	257	10.9	27.3
3- 4	314	13.2	40.5
4- 5	244	10.3	**50.8**
5-10	737	31.2	**82.0**
10-15	180	7.6	89.6
15-20	65	2.7	92.3
20-25	33	1.4	93.7
25-30	32	1.4	95.1
30-85	114	4.8	99.9
Total	2,365		

seem, then, that if the downward trend continues, no change in techniques will be necessary.

Since there is a possibility that the trend may not continue, it is worth while examining the 10-year mortality figures further, to determine whether a change to earlier immunization is warranted. So far as diphtheria is concerned, it will be noted in Table 4 that 50% of the deaths occur under the age of 5 years and that 82% occur under the age of 10 years.

The table also shows that the highest mortality among children under 5 is not in the first-year age group, as may have been assumed, but is in the 4-year-old group. Three hundred fourteen deaths occurred in the fourth year, whereas only 211 occurred in the first year; therefore less than 9% of the total diphtheria deaths occur in children under one year of age.

Among those less than one year old, however, half the deaths occurred before 4 months of age (Table 5). The worst ages for deaths in the first year of life are the second and third months, that is, before one could hope for good protection by active means, even if this were started on the first day of life.

Even allowing no time at all for the development of antibodies, if inoculations were started at 3 months, over 64% of deaths in the first year would occur before the customary three monthly inoculations were completed. If they are started at 6 months, only 12% more deaths might be expected to occur, that is, about 30 more deaths in 10 years, or 3 deaths in all of Canada in a year. The saving of even three lives a year, though minimal, is nevertheless an apparent advantage. This advantage, however, may possibly be offset by the lower percentage of protective titers [3] and the shorter duration of the protection [4] which can occur when active immunization is offered to very young infants.

TABLE 5.—*Deaths in Canada from Diphtheria in Children Under One Year Old 1939-1948*

Age, Mo.	No.	Per Cent	Cumulative Per Cent
0- 1	11	5.2	....
1- 2	35	16.6	21.8
2- 3	43	20.3	42.1
3- 4	18	8.5	50.6
4- 5	14	6.6	57.2
5- 6	15	7.1	64.3
6- 7	7	3.3	67.6
7- 8	13	6.2	73.8
8- 9	6	2.8	76.6
9-10	11	5.2	81.8
10-11	21	9.9	91.7
11-12	17	8.1	99.8
Total	211		

Very early active immunization against diphtheria is therefore probably not the answer to the problem of reduction in mortality in this disease. Better results might be expected if more effort were expended in so modifying existing immunization programs that the age groups with the highest mortalities, viz., 3, 4, and 5 years, would receive better protection. The immune responses of these children would not be hampered by any interference due to the presence of maternal passive antibody or due to "immaturity" of their immunity mechanisms. Furthermore, unlike those under 3 or 4 months of age, in all of these children there is hope of completing immunization before death intervenes.

With regard to the problem of whooping cough, Table 6 shows that of 4,001 deaths from whooping cough occurring in Canada over a 10-year period, 74% occurred in those under one year of age. Unlike diphtheria, whooping cough is a disease killing principally in the first year of life.

3. Cooke, J. V.: Antibody Formation in Early Infancy Against Diphtheria and Tetanus Toxoids, J. Pediat. **33**:141-146, 1948.

4. Di Sant'Agnese, P. A.: Combined Immunization Against Diphtheria, Tetanus, and Pertussis in Newborn Infants, Pediatrics **3**:333-444, 1949.

Although the literature is now replete with references to the possibility of obtaining "protective" agglutinin levels, the reports indicate that if infants are inoculated beginning at the age of 1 month instead of at the age of 7 months alum-precipitated preparations are to be preferred to the fluid variety.[5] According to the questionnaire referred to earlier, the alum-precipitated preparations are not used routinely by many Canadian municipal health departments and probably are not used routinely by most Canadian practitioners. Yet, in the light of the before-

TABLE 6.—*Deaths from Whooping Cough in Canada 1939-1948, Inclusive*

Age, Yr.	No.	Per Cent	Cumulative Per Cent
0- 1	2,992	73.9	73.9
1- 2	602	15.0	88.9
2- 3	187	4.6	93.5
3- 4	81	2.0	95.5
4- 5	46	1.1	96.6
5-10	68	1.7	98.6
10-15	14	0.3	98.3
15-90	11	0.3	98.9
Total	4,001		

TABLE 7.—*Deaths in Canada from Whooping Cough in Children Under One Year Old 1939-1948*

Age, Mo.	No.	Per Cent	Cumulative Per Cent
0- 1	155	5.2	....
1- 2	459	15.3	20.5
2- 3	469	15.7	36.2
3- 4	380	12.7	48.9
4- 5	285	9.5	58.4
5- 6	266	8.9	67.3
6- 7	216	7.2	74.5
7- 8	202	6.7	81.2
8- 9	165	5.5	86.7
9-10	152	5.1	91.8
10-11	134	4.5	96.3
11-12	109	3.6	99.9
Total	2,992		

mentioned reports, one naturally doubts the advisability of using fluid products as a routine public health procedure when immunization is begun early.

Let us assume, however, that the antigens used are the presumably superior ones which are available to most of those who are currently investigating this problem, that is, alum-precipitated and aluminum hydroxide (alhydrox®) preparations. Immunization programs starting at four different ages are currently being used against pertussis. Even if the antigen were 100% effective at all ages, which it is not, the following results might be expected from these four programs.

1. If one starts immunization in the seventh month of life, 67% of the first-year deaths will already have occurred before starting. If this age is used as a starting

5. Lapin, J. H., in Advances in Pediatrics, edited by S. Z. Levine, A. M. Butler; L. E. Holt, Jr., and A. A. Weech, New York, Interscience Publishers, Inc., 1949, Vol. 4, pp. 145-230.

point, it will take to the ninth month to complete the three monthly injections. Even if only one month is allowed for the development of protection, it will be seen in Table 7 that about 92% of the first-year deaths will have occurred by this time. (Maximum protection apparently does not occur before about two months following pertussis vaccination.[6])

2. Starting inoculation at 4 months, we can expect that 48.9% will have died before we begin, and 81% will die by the time protective immunity was beginning to be established. This is 11% less deaths than on the last schedule, a saving of about 320 lives in 10 years, or about 32 a year.

3. If 3 months is used as the starting age, 36.2% will have died before starting, and 74.5% before a protective level can begin to be obtained, that is, a saving of about 17.5% (92%— 74.5%), about 520 lives in the 10-year period, or about 52 a year.

4. Starting in the first month of life, we will have lost 48.9% before protection is obtained. This means a saving of 43%, about 1,287 in 10 years, or about 129 lives a year. This would be a substantial figure except that immunization, if started at this very early age, gives protection to only about 60%, which means about 78 infants.[4] (The use of a fluid vaccine might conceivably give an even lower number with protective levels.[7]) Furthermore, within a few months, about half of these have lost their protective immunity.[4] This leaves, therefore, a saving of lives of only about 40 a year. If one compares this with 146, which is the average yearly number of deaths before the age of 4 months in the 10-year period 1939-1948, it is seen that all the current methods are not solving the problem in a completely satisfactory manner. Indeed almost half the deaths in the first year occur at an age which is not likely to be affected by an early active immunization program.

The answer, therefore, might lie in passive immunization of very young infants. This could perhaps be accomplished by immunizing mothers in the prenatal period, as has been suggested by Cohen.[8] The objection that this passive immunity would interfere with active immunization of the infant fades into insignificance as far as pertussis is concerned, since a passively immune live infant is obviously better off than an infant who dies from pertussis because he lacks antibodies of any description. Since so many die in the first months of life, a procedure which could conceivably influence this mortality favorably should not be discarded as lightly as some would advocate.[5] However, since the clinical efficacy, as well as the duration of this passive immunity, has not yet been satisfactorily worked out, further modification and further study is certainly necessary before it can be universally accepted.

One must therefore draw the following conclusions with regard to mortality.

1. Any program which advises starting immunization of infants at an age earlier than, say, 6 or 7 months is not going to be a complete one. So far as diphtheria is concerned, no significantly favorable alteration in mortality figures can be expected.

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6. Sako, W., and others: Early Immunization Against Pertussis, J. A. M. A. **127**:379, 1945.

7. Sako, W.: Studies on Pertussis Immunization, J. Pediat. **30**:29-40, 1947.

8. Cohen, P., and Scadron, S. J.: Placental Transmission of Protective Antibodies Against Whooping Cough, J. A. M. A. **121**:656-662, 1943. Cohen, P.; Schneck, H., and Dubow, E.: Prenatal Multiple Immunizations, J. Pediat. **38**:696-704, 1951.

So far as pertussis is concerned, early immunization can influence mortality favorably, but it is not as great an influence as the protagonists for very early immunization would have us believe.

2. If one couples these observations with the fact that there has been a gradual decrease in total mortality from diphtheria and whooping cough, coincident with a conservative program, it becomes apparent that, unless something outstandingly better is forthcoming, a conservative approach to early immunization is still not unreasonable.

3. On the other hand, if early immunization is to be used, Canadian public health authorities might well reevaluate their present practice of using fluid antigens, in the light of the preference for alum-precipitated products expressed in the literature.

4. Finally, if mortality in the first year of life is to be reduced to a minimum, more attention should be paid to the possibilities of maternal (prenatal) immunization.

Paediatric Centre.

All tables were derived from data provided by the Vital Statistics Section, Dominion Bureau of Statistics, Ottawa, Ont., Canada.

CONSIDERATION OF ERRORS IN THE DIAGNOSIS OF INTUSSUSCEPTION

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AT THE Johns Hopkins Hospital in the period from 1939 to 1951 there have been five deaths from intussusception. In that time we have treated 79 children for this condition. The five deaths actually occurred in the first 40 of the cases, which were seen between 1939 and 1946. In analyzing our experience with intussusception,[1] we were chagrined to discover that in each of these five cases a serious delay had occurred in the initiation of definitive treatment. In each instance the delay was caused by failure to diagnose the intussusception upon the patient's first visit to the hospital after the onset of the condition. In one child, intussusception was only an incident in the course of an already-established fatal disease, but the other four children should not have died had the diagnosis been made promptly.

The experience has led us to review the histories of the children in whom intussusception was improperly diagnosed at The Johns Hopkins Hospital in the period 1930-1951, in order to emphasize, if possible, the more common diagnostic pitfalls.

By and large, intussusception is a readily diagnosed disease with an easily recognized symptom pattern. Characteristically, intussusception attacks well-nourished boys 5 through 9 months old. It is well to note that in many children the symptoms and signs of intussusception supervene during a mild illness, such as an upper respiratory infection or a bout of nonspecific diarrhea. Those who feel that the presence of enlarged submucosal lymphoid masses predisposes to intussusception [2] see a causal relationship here. A few patients have strong and clear histories of previous similar attacks from which they recovered spontaneously. Such a history therefore should sharpen suspicion, not allay it.

The typical attack of intussusception begins with sudden onset of abdominal pain. The child cries out, writhes, may vomit, and is suddenly well only to be seized again 15 or 20 minutes later. This time he may evacuate a normal stool. The attacks of pain and vomiting increase in frequency. The child is generally drowsy and listless, but at times he may be playful between bouts of colic and at times restless and fretful. Feedings may be accepted but are usually not retained. There may be a

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1. (*a*) Ravitch, M. M., and McCune, R. M. Jr.: Reduction of Intussuception by Barium Enema, Ann. Surg. **128**:904-917, 1948; (*b*) Intussusception in Infants and Children, J. of Ped. **37**:153-173, 1950.

2. Dennison, W. M.: Acute Intussusception in Infancy and Childhood, Glasgow M. J. **29**:71-80, 1948. O'Sullivan, W. D., and Child, C. G., III: Ileocecal Intussusception Caused by Lymphoid Hyperplasia, J. Pediat. **38**:320-324, 1951.

second stool without blood, after which blood and mucus are all that is discharged. This is the typical picture and a brief review of the incidence of the various symptoms may be worth while.

Pain is the commonest initial symptom, occurring in 47% of 152 cases studied at The Johns Hopkins Hospital. Vomiting is the next commonest initial symptom, occurring in 36%. Bloody rectal discharge, as an initial symptom was noted in 11%, mostly infants in whom the earlier symptoms were presumably overlooked. In 6% of the 152 children, refusal to eat was the initial symptom. A large variety of other symptoms heralded the onset, in a few children each—prolapse of the intussusception, restlessness, diarrhea, constipation, distention, apathy, fever, and convulsions.

As far as concerns the occurrence of the various symptoms at one time or another during the illness, the following data are of interest. Ninety-three per cent of the children had vomited before treatment was begun, most of them in the first three hours, and this was particularly true of the infants (73%); pain at some time was attributed to 91% of the children over 2 years old, to 82% of the infants 1 to 2 years old, and to 61% of the infants under 1 year. Blood, at some time, if only upon rectal examination, was seen in 91% of cases, with a considerable difference between infants and older children (95% of those under 2 years old, 65% of those over 2 years old). Sixty per cent of those who showed blood did so in the first 12 hours, and 37% in the first three hours. A few white blood cells were occasionally seen upon microscopic examination of the rectal discharge, but pus was rare. It is to be emphasized that in a good number of cases the first blood seen was on the examining finger.

Diarrhea during the period of intussusception occurred in 11, or 7.2%, of the 152 cases, and 9 of these 11 were under 1 year old. This is of extreme importance, for there is an understandable tendency to assume that in the presence of intussusception there must be complete intestinal obstruction. Of these 11 children, the condition was actually mistakenly diagnosed in 5 as dysentery, and 3 subsequently died as a result of the delay.

Upon physical examination, a significant elevation in temperature at the time of admission was found in almost half the children in the group; occasionally there was very high fever. A moderate leucocystosis was common, and high counts were not rare. Just under half (48%) showed evidences of prostration, generally directly related to the duration of symptoms. Similarly, dehydration was obvious in 41%.

Examination of the abdomen, and rectal examination are the most important features of the bedside diagnostic procedure. The abdomen is usually flat or scaphoid, relaxed, soft, and nontender. The intussusception may form a visible mass. There may be slight tenderness or minimal resistance directly over the mass. Palpation of the mass itself is pathognomonic. The mass may be difficult to feel when the intussusception passes into the hepatic flexure and is behind the costal margin and the right lobe of the liver. Later on, the nonspecific signs of intestinal obstruction, that is, distention and intestinal patterns, may obscure the mass and make it impossible to feel. A mass was felt by abdominal or rectal examination in 89%. In six cases rectal examination revealed a mass not felt by abdominal palpation. Abdominal resistance was noted in 40% of cases and tenderness in only 41%, while 60% of

cases showed complete relaxation of the abdominal wall, with no resistance or spasms anywhere. Distention was remarked upon in 35%.

In the last 21 years, 98 children with intussusception have been treated at The Johns Hopkins Hospital. In 19 of these there was an initial error in diagnosis, which affected the treatment, and 8 of these 19 children died.

With these facts, and bearing in mind the pattern of history and physical examination in ordinary cases of intussusception, we may proceed to an analysis of the cases in which there was a diagnostic error with a significant ensuing delay. A study of this kind obtains its chief value from an examination of the clinical characteristics of the cases reviewed and does not lend itself to statistical tabulation, so that it seems most profitable to discuss the cases in groups, using individual cases for illustration.

Our errors in making the diagnosis have fallen into several categories. One case was that of a patient who showed all or most of the signs of intussusception, which was not recognized because of the ignorance of the examining physician. In a second group the diagnosis was missed because of the duration of the symptoms and the relative well-being of the child. There were five such cases. In all of them the diagnosis was not entertained because the history went back for periods varying from a week to as much as 40 days during which the general condition of each child remained good. Finally, in each instance admission was precipitated by the worsening condition of the child. One must ever keep in mind the occasional occurrence of "chronic," nonstrangulating, incompletely obstructing intussusception.

The age of the patient was misleading to the pediatrician in several instances. Of the total group of 19 patients whose condition was initially misdiagnosed, there were 8 patients over 1 year old, including 6 over 2 years, and there was 1 who was 2 weeks old. Of 152 cases previously reported [1b] almost 90% were under 2 years old. In this group of 19 children, 6, or nearly one-third, were over 2 years old. One tends to forget the possibility of intussusception in the older age groups, as well as in newborn infants.

One of the commonest errors was in making the diagnosis of dysentery, based upon fever, vomiting, bloody stools, and abdominal pain. In this series, there were five cases in which the erroneous diagnosis of dysentery was made. When one considers how common dysentery is and how variable its manifestations, it is no wonder this error was made. One can only suggest that intussusception must be kept in mind.

In two cases there was sufficient spasm, rigidity, and tenderness to simulate an acute abdominal condition requiring surgery. In one, a diagnosis of appendicitis seemed unequivocal, with tenderness and spasm in the right lower quadrant, no palpable mass, and no bloody stool. Upon operation the appendix was found to be normal, and intussusception was found. In the other case there was first tenderness in the right upper quadrant, then considerable rigidity, and consequently the possibility of appendicitis, sickle-cell crisis, or other cause of abdominal pain and spasm was entertained. Eventually, after administration of secobarbital (seconal®) sodium, a mass was felt and the diagnosis made by barium enema. It is worth remembering, therefore, that abdominal spasm may be an important feature of these cases and may prevent early palpation of the mass.

Palpation of the intussuscepted bowel should not be considered a *sine qua non* for the diagnosis. In this group of 19 cases there were 8 cases in which no mass

was ever felt by abdominal palpation or by rectal examination and 8 cases in which there was a variable delay in its palpation. In one case a palpable "liver" was repeatedly mentioned. This may possibly have been the intussusception. In some cases the mass was undoubtedly under the costal margin and therefore not palpable. In others it may have been obscured by distention and in still others by tenderness and spasm. In 7 of the 19 cases, the intussusception involved the ileum only. In four of these, no mass was ever felt, while among those in which a mass was ultimately palpated only one patient had an intussusception involving the ileum alone.

Blood in the stools or currant-jelly stools is another classic sign of intussusception. That it may not appear in an appreciable number of cases is evident, since it did not appear at all in 10 of our 19 undiagnosed cases. Indeed, in several cases the stools were normal or nearly so, and in some others there were repeated watery stools. In some cases there was occult blood in the stools, and in others it was found only by rectal examination.

In two cases and possibly in a third, the issue was beclouded because the patients were already in the hospital with another disease.

Occasionally a blatantly typical case is misdiagnosed, as in the following instance.

P. G., a 10-month-old white girl, was seen in the dispensary with a temperature of 101.8 F. and a history of fever, vomiting, and constipation for over 24 hours. An enema the night before had returned bright red blood. The abdomen was distended, and there were "no fecal masses, no tenderness, masses, or spasms." Enema return in the dispensary was "practically clear except that the water was tinged with light pink." Diagnoses were "otitis media, chronic constipation, (?) intussusception." The child was sent home to return the next day. However, the error was detected that night by the dispensary chief in a review of the day's histories, and the baby was found and brought in 12 hours after the first dispensary visit. The child was now flaccid and almost completely unresponsive. A diagnostic barium enema filled the colon. Roentgenograms showed numerous loops and fluid levels, and, upon operation, a short intussusception was found just above the ileocecal valve. It was not gangrenous but was irreducible. Resection and anastomosis were performed. The child's temperature rose to 40.4 C. (104.8 F.). She had convulsions for six hours and died. The specimen showed the intussusception to have been due to a nodule of aberrant pancreatic tissue.

This child had vomiting, constipation, and blood in the bowel when first seen, and intussusception had to be considered, regardless of the absence of a mass, which was all that was lacking. If the mere thought of intussusception is entertained, a barium enema should be administered, and only if the small bowel fills readily and there are no fluid levels or distended loops may the possibility be dismissed. It is true that in this instance the intussusception was entirely in the small bowel, which makes for more difficult diagnosis and higher mortality. There was one other case of essentially inexcusable diagnostic inaccuracy which fortunately resulted in recovery.

While everyone may at times fail to see the obvious, a high index of suspicion in regard to intussusception, and a sense of urgency in the presence of the possibility of intussusception, should reduce the number of diagnostic errors. It is possible in some of the cases to see how the examiners were misled.

In five cases the duration of the illness was so long and the children in such good condition that the correct diagnosis was not entertained until late. These cases were of very different types.

The first case was that of a 6-year-old child with a two-year history of anemia, abdominal pain, anorexia, and tarry stools, with occasional vomiting. She had frequent attacks of abdominal

pain when a mass was visible in the abdomen. Even though these attacks occurred during a hospital admission, intussusception seems not to have been considered. Laparotomy was finally undertaken, and two separate intussusceptions were found, with polyps in each small bowel area.

This child had peculiar pigmentation (Hutchinson-Jeghers-McKusick spots) on the lips, the significance of which,[3] as indicating diffuse intestinal polyposis, was not then realized. The chronicity of her complaint and the extensive blood loss due to the polyps had led to diagnoses of Meckel's diverticulum, ulcerative colitis, etc.

Another patient, whose case is celebrated in the annals of the Harriet Lane Home, was an 8-month-old Negro girl whose initial dispensary visit was on the 14th day of illness. This had begun with abdominal pain and a normal evacuation, followed after five hours by the passage of blood. She vomited every day, had fever every day, and had one or two normal stools every day until the day of her first visit, when she had a bloody, watery stool. Examination showed dehydration, a palpable liver, a fluid brown stool, and blood in the rectum. She was thought to have dysentery and was followed thereafter for 40 days, during which she made repeated dispensary visits. Sometimes she had diarrhea, sometimes not; sometimes she vomited, sometimes not; sometimes she passed blood, sometimes not. She never failed to have a stool, but often had bouts of pain. The "liver" was usually palpable.

She was finally admitted to the hospital where, after three days, a barium enema was given as part of the diagnostic study and was interpreted as normal. The next day when regular rounds were made, a mass was finally felt. Barium enema reduced a typical intussusception from the transverse colon to the ileocecal valve, and reduction was completed at operation. The child had no trouble thereafter. Review of the roentgenograms, which had been read as normal, actually shows a typical "chronic" intussusception (Fig. 1).

In this instance, despite innumerable bloody stools, bouts of pain, and vomiting, the possibility of intussusception was ignored because of the long history in an 8-month-old infant who was obviously not desperately ill.

The next child in the group with chronic intussusception was a one-year-old Negro girl with vomiting and constipation of one week's duration and with a history of flecks of blood in an enema and repeated bouts of periodic abdominal cramps. The abdomen was distended, a roentgenogram showed dilated loops, and intestinal obstruction was suspected, but because her conditions seemed "exceptionally good" she was sent home to return the next day. She was then distended; there was tenderness and spasm in the right lower quadrant and the suggestion of a mass. She was thought to have a low intestinal obstruction. Barium enema showed an intussusception in the right lower quadrant for which operation was undertaken, the intussusception being reduced.

In this instance, the picture was largely that of intestinal obstruction, for which admission and operation should have been advised in any case.

The fourth case of delayed diagnosis in a child with a long history was that of a 2½-year-old white girl who had a 10-day history of illness. She had begun with sudden severe cramps which persisted at frequent intervals. She vomited after almost every meal, no blood was seen, and she had normal stools for the two days preceding admission. She was thin, dehydrated, and crying with frequent spasms of abdominal pain. There was much audible peristalsis. Hard dried feces lay in the rectum. There was tenderness and muscle spasm in the right upper quadrant and a poorly defined tender mass. She was observed for 12 hours for "(?) lead poisoning, (?) appendiceal abscess," until a diagnostic barium enema showed an intussusception at the hepatic flexure. Operative reduction was successful.

There seems little justification for the delay in operation, although the absence of bleeding and distention are extenuating factors, and although the mass must have been partly concealed by the liver and the right costal margin.

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3. Ravitch, M. M.: Polypoid Adenomatosis of the Entire Gastro-Intestinal Tract, Ann. Surg. **128**:283-298, 1948.

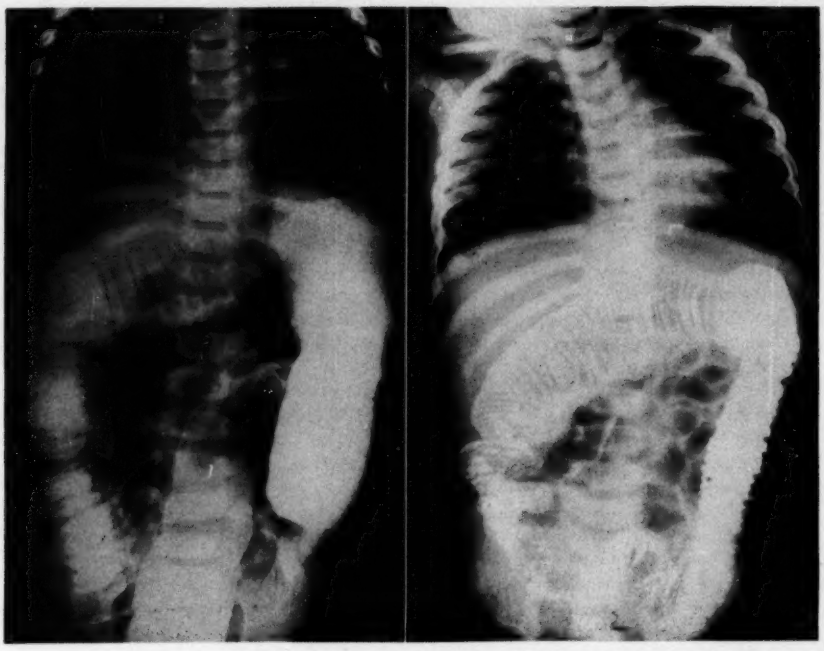

Fig. 1.—Roentgenograms of barium enema of 8-month-old infant with chronic intussusception. This child was followed at frequent intervals for over a month, with inconstant symptoms of diarrhea, abdominal pain, blood in the stools, vomiting, and "palpable liver." These roentgenograms were not actually diagnosed as intussusception, the diagnosis being made three days later by palpation of a characteristic mass. Intussusception need not cause complete intestinal obstruction, and chronic intussusception may occur.

The "coiled spring" appearance is typical of chronic intussusception and is produced by the thin layer of barium between the sheaths of the intussusception. The pull of the mesentery holding the bowel causes the reefing of the bowel, which is responsible for the ring-like shadows.

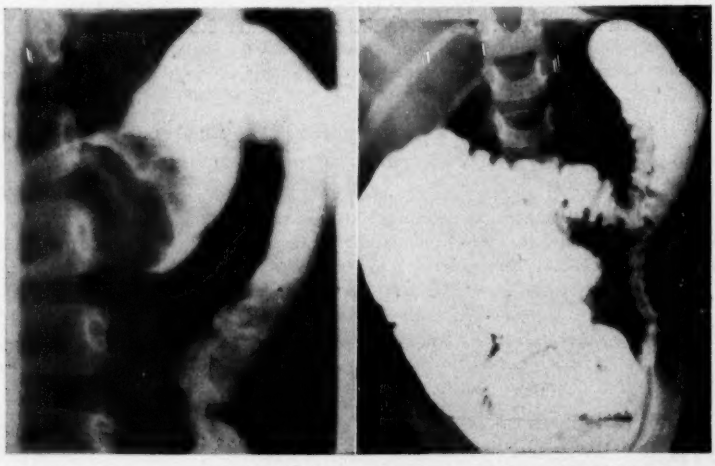

Fig. 2.—Roentgenogram of typical intussusception in a 3¼ year old child with symptoms of 17 hours' duration. *A*, the advancing barium column meets the sharply outlined intussusception producing the characteristic concave meniscus. Notice the difference between this and Figure 1. *B*, complete reduction of the intussusception with filling of many loops of small bowel by the barium enema. In 45 of 60 patients treated primarily by barium enema since 1939 the barium enema has affected complete reduction. There have been no deaths in the series.

The last child in this group was a 6-month-old white boy with a three-week history of cramps and vomiting, occurring in episodes. He had daily stools and never passed blood. Three days before admission a tubular nontender mass in the left upper quadrant was felt and taken to be a duplication of the colon. Upon operation this mass proved to be an intussusception at the splenic flexure. When it was reduced, a small mass at the ileocecal junction was discovered and resected and turned out to be a small duplication which had led the intussusception.

The most interesting feature common to all these five children is that, despite the fact that they had long-standing intussusceptions varying in duration from 10 days to a month and more, all survived and none had gangrenous bowel. This is inherent in the nature of chronic intussusception. A moment's reflection will show that precisely those children will have chronic intussusception of long standing whose intussusceptions do not become gangrenous and in whom neither the intestinal canal nor its vascular supply becomes completely obstructed. One should not insist upon feeling a mass before resorting to barium enema. The mere fact of a long history in a child who is still in tolerably good general condition does not exclude intussusception, and the child may continue to pass stools daily. By the same token, in these cases bleeding into the bowel may be inconspicuous or absent.

A very small group is represented by two children who were already in the hospital and seriously ill when intussusception supervened.

An 18-month-old white boy, whose case has been reported elsewhere,[3] was in the hospital dying of malnutrition as a result of diffuse polyposis of the entire intestinal tract. This had resulted in almost constant diarrhea. In the ward, a long time after admission, he "spent a bad night with abdominal pain" and began to pass liquid, bloody stools. After 24 hours a mass was felt in the right upper quadrant. The mass developed rapidly. It was explored and found to be an ileoileal intussusception. The child died 24 hours after operation. At autopsy the entire bowel, from cardia to anus, was found to be studded with these polyps.

A 9-month-old Negro girl was admitted with a two-week history of green diarrheal stools, blood in stools, fever, cough, and persistent vomiting. There was right-upper-quadrant pneumonia. The child was very dehydrated; the eyes and the fontanelles were sunken. The abdomen was scaphoid. The temperature was 40.8 C. (105.4 F.). The abdomen became tympanitic and distended almost at once, and she began to pass gross blood in the stools, with much mucus. After 72 hours she was markedly distended and sicker, despite clearing of the pneumonia. Barium enema was normal, but she was having repeated currant-jelly stools. Upon operation, a necrotic ileoileal intussusception was found and resected, death eventuating.

In both these instances, intussusception developed in a child already seriously ill, and the diagnosis was delayed because the child was already in the hospital on another account. Members of the staff were slow to appreciate the significance of the change in symptomatology.

The largest group and the most deceptive consists of the babies who were at first thought to have dysentery and finally were found to have intussusception. There were six of these children. When the variable character of early dysentery in infants and children is remembered, this error does not seem so remarkable, although again it would be preferable to conduct more barium-enema studies.

A 10-month-old baby was admitted to the dispensary with a temperature of 103.4 F., after 24 hours of vomiting while the stools were normal. The throat was red, the eyes sunken, and the child was restless. She was treated for dysentery in the prediarrheal stage. The next day, with a temperature of 106.6 F., she was admitted to the hospital. She was very well nourished and seemed fairly well. There were tenderness and resistance in the right upper quadrant. She was thought to have a paralytic ileus of unknown origin. Roentgenograms showed dilated loops. Two days after admission, laparotomy showed a gangrenous intussusception, which was resected. The child died soon after.

In this instance obesity of the child interfered with abdominal palpation and with accurate assessment of the condition. There appeared, from the record, to be a constant search for real abdominal rigidity in a 10-month-old infant. It is well known that in young infants there may be little or no resistance to acute abdominal lesions. The presence of constipation, distention, and vomiting were not properly evaluated.

The next child also died. He was a 6-month-old infant with a 48-hour history of bloody stools, vomiting, and crampy abdominal pain. He was in shock, bleeding from the rectum, and severely dehydrated. Rectal examination showed bloody mucus. It was discovered that the child had been offered egg for the first time on the day of onset, and therefore time was taken to test his allergy to egg albumin, which proved minimal. Roentgenograms showed dilated loops, and after several hours operation was undertaken. At operation an ileoileal intussusception was discovered. Temperature rose to 41.6 C. (106.8 F.), and he died, perhaps as a result of scanty supportive treatment, having received only a little dextrose before the operation and only 100 cc. of blood after the operation.

In this instance a delay of a few hours was occasioned by neglect of the obvious indications of intussusception with a clear clinical picture except for absence of a mass. The intussusception was ileoileal. The time which was wasted could have been employed in vigorous transfusion therapy.

The third child mistakenly thought to have dysentery was 8 months old. He came to the hospital shortly after having passed four watery yellow stools and vomited several times. He was obviously acutely ill and was sent home as having dysentery. Next day he appeared to be having cramps and had a bloody mucous stool. There was now a mass in the right upper quadrant. Barium enema reduced a typical intussusception to the right colon, whence reduction was completed at operation.

The fourth infant in the dysentery group came to the dispensary after 18 hours of vomiting and no stool. He was thought to have an "acute nutritional disturbance"; he was given fluids intravenously, and feedings were ordered withheld. Several hours later he was brought back with colicky pain and a right-upper-quadrant mass; there was blood on the finger after rectal examination. Barium enema reduced the intussusception to the cecum, and operation completed the reduction.

In this case vomiting and the fact that the child had been one day without a stool were all there was to arouse suspicion, but a barium enema might have been advised because of the question of intestinal obstruction.

The fifth child in this group, an 8-year-old Negro boy, had a 10-hour history of severe cramps, with vomiting and several watery stools with mucus and blood. The abdomen was rounded and slightly distended. Rectal examination yielded a liquid stool with blood, mucus, and white blood cells. The diagnosis upon admission was dysentery, but after several hours a barium enema was done which showed an intussusception in the descending colon, which was readily reduced by hydrostatic pressure.

The last child in this group was a 7-month-old white girl with a two-week history of vomiting, having 10 to 12 diarrheal stools a day, fever, and anorexia. Blood appeared in the stools the day before her first visit, and on that day she had only 3 to 4 stools. The temperature was 101.4 F. She was irritable, toxic, and slightly dehydrated, and the ear drums were red and bulging. The "liver" was felt 2 cm. below the costal margin. A myringotomy was done, and she was sent home. The next day she was vomiting and had a loose purulent stool, a tender abdomen, and a rectal prolapse. She was admitted, and the next day a barium enema showed a normal colon; but distention increased and stools ceased altogether. At operation an ileoileal intussusception was reduced. The child seemed to be recovering when colon bacillus meningitis developed and she died.

Her cramps, vomiting, and tenderness had been ignored, and it is possible that the "liver" was the intussusception.

At least three children suffered a delay in diagnosis because of a compound error: It was thought that some other form of mechanical intestinal obstruction was present, yet the child was not admitted to the hospital for immediate operative treatment.

One child of 6 years was seen after 48 hours of periumbilical pain and considerable vomiting, with no stool in the second 24 hours. The "liver" was thought to be palpable. An enema was ineffectual, but the child was sent home. He was brought back the next day markedly ill, dehydrated, and distended, with numerous dilated intestinal loops. It was thought that he might have peritonitis and ileus, but operation showed a large ileocecal intussusception which was resected, and death followed soon after operation.

A 4-year-old boy with a similar history was more fortunate. He had a two-day history of abdominal cramps, was sent home, and returned in 24 hours, having vomited several times. There was a little spasm in the right upper quadrant and active peristalsis. He was sent home again and returned the next day with cramps, distention, and right-upper-quadrant tenderness and spasm. With the child under sedation with secobarbital (seconal®) sodium, a typical intussusception was felt. Barium enema reduced it to the cecum, and operation completed the reduction.

In this instance the boy was twice sent home, despite right-sided abdominal tenderness and a history of cramps.

By contrast with these cases there is the following case history.

A 3½-year-old white boy had a 12-hour history of generalized abdominal pain, nausea, and vomiting, with no stool in that time. There were tenderness and rigidity in the right lower quadrant. Operation for appendicitis was promptly undertaken. An intussusception was found to have passed into the ascending colon, and reduction and cure were readily accomplished.

Intussusception had not been suspected, and no barium enema was performed, but operation was undertaken without delay and the result was good.

There was one fatal case in which we see no opportunity for the diagnosis to have been made.

A 2-week-old infant with diarrhea had been having up to 7 or 8 stools a day since the second or third day of life. There had been no vomiting and no blood in the stool. He had taken feedings until four days preceding admission. The abdomen was soft. There was no vomiting and no distention. At autopsy a gangrenous intussusception in the midileum was found.

It is worthy of note that in 7 of the 19 cases of misdiagnosed intussusception, the intussusceptions were definitely ileoileal and had not yet involved the colon. This being a disproportionately high figure in view of the low incidence of such intussusceptions in the entire series, it must be assumed that there is a direct connection between the occurrence of ileoileal intussusception, the difficulty in diagnosis, and the high mortality. There have been 16 deaths in the 98 intussusception cases since 1930, and in 8 of these the intussusceptions were ileoileal. The incidence of intussusceptions beginning high in the small bowel was 10% or less in the entire series, further emphasizing the special character of such intussusceptions.

SUMMARY

Errors in diagnosis of intussusception occurred in at least 19 cases in our hospital since 1930; these errors were associated in 18 cases with significant delay in treatment. In the nineteenth case appendicitis was thought to be present, and

upon operation the intussusception was found and relieved. Errors in diagnosis were based on a number of misconceptions. In some cases a history of days or weeks of pain, vomiting, constipation, etc., with relative well-being, was not recognized as characteristic of chronic, nonstrangulating intestinal obstruction. In six cases the passage of feces, even to the point of diarrheal stools, was enough to lead the examiners astray with the suspicion of dysentery. In several cases intestinal obstruction of uncertain type was thought to exist, but operation was not immediately undertaken. On the one hand, in many of the cases too much stress was laid on failure to feel a mass, while on the other hand, an enlarged "liver" was palpated in several cases, and insufficient weight was attached to a finding of slight abdominal tenderness or resistance. In some cases the absence of currant-jelly stools apparently encouraged delay, but in others pink enema returns or a history of blood in the stools failed to alarm the observers.

If we are to lose no children from intussusception, early accurate diagnosis is required. This calls for a high measure of suspicion and a ready resort to barium enema and plain roentgenograms of the abdomen in doubtful cases. A barium enema which runs into the distal ileum rules out the ordinary type of intussusception at the ileocecal valve but does not rule out one higher in the ileum. The latter will usually show distended, gas-filled loops in the roentgenogram. Mechanical intestinal obstruction from any cause requires early relief by operation, and alertness to advise early operation for suspected intestinal obstruction will benefit the patients with obstruction far more than it will harm the occasional patients who will prove to have been unobstructed. Had this practice been followed in the cases reported above, it might have saved a number of children in whom intussusception produced a picture of intestinal obstruction, the importance of which was minimized.

HEMOGLOBIN, RED CELL COUNT, AND MEAN CORPUSCULAR HEMOGLOBIN OF HEALTHY INFANTS

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THE CHANGES in composition which the blood of infants undergoes during the first year of life have been extensively investigated. The excellent reviews of previous studies, included in the reports by Mackay (1931) [1] and Faxén (1936-1937),[2] obviate the necessity of a survey of the literature in the present paper. These reviews point out the many factors which have been suggested as influencing the blood picture and suggest that hypochromic anemia may be a common occurrence in young infants. Considerable doubt remains, in consequence, as to what constitutes the normal blood picture in infants and what may be considered as the limits of physiological variation.

The present study was undertaken for the purpose of helping to establish normal hematologic standards for infants residing in Minnesota and of investigating the influence of certain factors on the blood picture.

PROCEDURE

The study was conducted at two well-baby clinics in St. Paul and one in Minneapolis and included infants from 1 to 12 months old. The two St. Paul clinics chosen for the study were ones in which experience had shown that the mothers were especially cooperative. The subjects selected by the attending physician included those infants born at term who were apparently in good health. In the Minneapolis clinic the public health nurses were responsible for making arrangements with the mothers for the blood tests. With few exceptions the Minneapolis families lived in University Village and the fathers were war veterans who were students at the University of Minnesota. In all the clinics the mothers were instructed to bring the infants for examination by the clinic doctor at regular intervals. The plan was to secure a continuous blood record for each infant during the first year of life, but in many cases only one or two observations were made because the infants did not return to clinic. The number of different infants studied and the total number of observations made at each clinic are given in Table 1. The average number of observations per subject was slightly less than two; the range was from one to seven.

From the University of Minnesota.

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1. Mackay, H. M. M.: Nutritional Anaemia in Infancy, Medical Research Council, Special Report Series, No. 157, London, His Majesty's Stationery Office, 1931.

2. Faxén, N.: The Red Blood Picture in Healthy Infants, Acta paediat. (Supp. 1) **19**:1-142, 1936-1937.

Blood samples were secured from a free-flowing finger or thumb puncture. Hemoglobin determinations were made in duplicate; the alkaline hematin method and National Bureau of Standards certified hemoglobin pipettes were used. Readings were made in a photoelectric colorimeter which had been calibrated by means of the Van Slyke and Neill oxygen-capacity method. For erythrocyte counts, duplicate readings were made on each of two dilutions; National Bureau of Standards certified Trenner automatic pipettes were used, and Gower's solution was the diluting fluid. The pipettes were agitated for at least five minutes in a mechanical shaker before filling the two sides of the counting chamber. All counts were made by skilled medical technologists.

The data were accumulated over two years which were separated by a four-year interval. During 1945-1946 the study was conducted only at the Central Clinic in St. Paul; during 1949-1950, at Central and St. John's Clinics in St. Paul and at University Village Clinic in Minneapolis.

The methods of statistical analysis employed were Student's *t* test of significant difference, analysis of variance, and correlation. The formulae used were those in general use.

RESULTS AND COMMENT

Because of the lapse of time between the two years of the study, it was decided to test statistically whether or not the two groups were homogeneous and might be

TABLE 1.—*Summary of Observations on Infants One to Twelve Months Old*

Clinic	Year	Boys		Girls	
		Subjects, No.	Observations, No.	Subjects, No.	Observations, No.
Central, St. Paul	1945-1946	24	49	27	46
Central, St. Paul	1949-1950	33	61	22	53
St. John's, St. Paul	1949-1950	36	83	31	70
University Village, Minneapolis	1949-1950	57	94	37	61
		150	287	117	230

considered as having been drawn from a single population. The hemoglobin values secured at Central Clinic (St. Paul) were used for this purpose. Although the age distributions of the infants were not the same in the two years, they appeared to be sufficiently similar to justify testing the significance of the observed differences. The results show that in the first year of the study, for both boys and girls, the mean hemoglobin value was slightly, but not significantly, lower than in the second year. For the boys, the mean hemoglobin value in 1945-1946 was 11.74 gm. per 100 ml. of blood and in 1949-1950, 11.90 gm. For the girls, the corresponding values were 12.09 gm. and 12.34 gm., respectively. It should be pointed out that, because of the great individual variation and the limited number of observations, the significance of small fluctuations in the amount of hemoglobin is difficult to demonstrate. It seems possible that the slightly higher hemoglobin levels in the second year were the result of the more liberal feeding practices followed in that year. In general, in 1945-1946 the practice was to add orange juice and vitamin D to the diet at two weeks, cereal or potato at three months, egg yolk and vegetables at four to five months, and liver and fruit pulp at six months. In 1949-1950, depending on the child's needs and development, cereal or potato, egg yolk, and vegetables were added as early as the third month, and liver, fruit pulp, and cottage cheese by the fourth or fifth month.

It seemed essential also to establish the homogeneity of the samples drawn from the three clinics in the second year of the study, since most of the families in the Minneapolis clinic were of a somewhat different social level from those in the St. Paul clinics. A comparison of the mean hemoglobin values given in Table 2 shows that, for both boys and girls, a slightly higher value was obtained for the infants at the Minneapolis clinic than for those at either of the St. Paul clinics. None of the differences between clinics was significant, although that between boys from the University Village and the Central Clinic just failed of significance at the 5%

TABLE 2.—*Mean Hemoglobin Values (1949-1950) for Infants from Three Well-Baby Clinics*

	Clinic		
	University Village	Central	St. John's
For boys, gm./100 ml.	12.23	11.91	11.95
For girls, gm./100 ml.	12.44	12.34	12.23

TABLE 3.—*Hemoglobin, Red Blood Cell, and Mean Corpuscular Hemoglobin Values for Infants from Three Well-Baby Clinics in Minneapolis and St. Paul*

	Boys						Girls					
		Hemoglobin, Gm./100 Ml.		Erythrocytes, Millions/ Cu. Mm.		Mean Corpuscular Hemoglobin, Micro-micrograms			Hemoglobin, Gm./100 Ml.		Erythrocytes, Millions/ Cu. Mm.		Mean Corpuscular Hemoglobin, Micro-micrograms	
Age, Mo.	Observations, No.	Mean	S. D.*	Mean	S. D.*	Mean	S. D.*	Observations, No.	Mean	S. D.*	Mean	S. D.*	Mean	S. D.*
1- 2	28	12.38	1.49	3.83	0.50	32.54	3.51	18	12.95	1.50	4.12	0.73	31.85	3.23
2- 3	38	11.23	0.70	3.75	0.54	30.42	4.14	28	11.50	0.80	3.84	0.51	30.39	4.08
3- 4	30	11.97	0.83	4.27	0.82	28.71	4.17	30	12.15	0.63	4.18	0.47	29.39	3.42
4- 5	32	12.14	0.80	4.61	0.61	26.67	2.96	25	12.60	0.67	4.49	0.50	28.41	3.41
5- 6	30	12.23	0.88	4.75	0.62	26.00	2.64	24	12.67	0.81	4.62	0.62	27.83	3.69
6- 7	24	11.83	0.79	4.55	0.87	26.79	4.69	18	12.25	0.72	4.58	0.68	27.18	3.34
7- 8	26	11.92	0.96	4.76	0.73	25.47	3.48	16	12.12	0.85	4.67	0.53	26.21	2.90
8- 9	17	11.97	0.92	5.08	0.76	23.96	3.38	21	12.34	0.83	4.59	0.51	27.19	3.36
9-10	14	11.92	0.55	4.68	0.96	25.51	1.52	17	12.36	0.55	4.79	0.54	26.08	3.06
10-11	16	12.06	0.91	4.45	0.74	27.09	4.33	16	12.03	0.86	4.54	0.75	27.18	4.48
11-12	22	12.17	0.80	4.75	0.47	25.84	3.10	10	12.50	0.54	4.58	0.57	27.64	3.00
12-13	10	12.52	0.92	4.89	0.59	25.85	2.72	7	12.06	0.50	4.89	0.65	24.94	2.53
	287							230						

* Standard deviation.

level. These statistical findings justified combining the data from the three clinics for the two years of the study.

In Table 3 are given, by age groups, the means and standard deviations for the hemoglobin, the red blood cell, and the mean corpuscular hemoglobin values for the boy and girl infants. Inspection of these data shows that the mean hemoglobin values for the boys range from 11.23 to 12.52 gm. per 100 ml. of blood, and for the girls from 11.50 to 12.95 gm. For red blood cell counts the range for the boys is from 3,750,000 to 5,080,000 per cubic millimeter, and for the girls, from 3,840,000 to 4,890,000. The low point for both hemoglobin and red blood cell counts occurs in the 2-month-old infants. Thereafter a gradual rise in values is noted, followed by a second decline in hemoglobin in the seventh month of life, with an even lower level for the girls in the eighth month. From this point on, there appears to be a gradual increase in both hemoglobin and red cell counts. The irregularity of

the increase is probably attributable to the small number of observations in the older age groups. The hemoglobin values in the present investigation compare favorably with those reported by Elvehjem and his associates (1933),[3] Mugrage and Andresen (1936),[4] and McNamara and Senn (1940).[5] These workers reported that the low point in hemoglobin level occurred between 2 and 4 months of age, with a moderate recovery thereafter. In their series, Mugrage and Andresen observed a short rise to 8 months and a secondary fall to 18 months. Faxén, working in Gothenburg, Sweden, with a carefully selected group of infants, secured hemoglobin values which were appreciably higher than those obtained in the present study. In one-month-old infants, Faxén secured a mean hemoglogin level of 17.9 gm., compared with a mean in the present study of about 12.5 gm. His low point, which came at 3 months, was 12.7 gm., with a moderate increase from 3 to 5 months of age. The level remained stationary at about 13.0 gm. or a little higher for the remainder of the first year. In red blood cell counts, on the other hand, little difference between the two studies is apparent, the values in the present study, especially in the second half of the first year of life, being slightly but consistently higher than those in the Faxén study.

A part of the difference in hemoglobin values in the two studies, at least in the younger age groups, is attributable to the difference in the bases used in setting up the various age groups. Faxén states that in his study the time for taking the specimen of blood was chosen in such a way that the range of the groups was as small as possible and the variations in the children's ages amounted to only a few days (seven at the most) from the center of the class. In the present study, there was as much as 30 days difference in the ages of the infants in each age group, and, provided the cases were evenly distributed throughout the range, the mean age of the infants in each group was in the middle of the range or, on the average, one-half month older than those in Faxén's age groups. Furthermore, he included in his study only breast-fed infants, and they, according to Mackay (1933),[6] have somewhat higher hemoglobin levels than do artifically fed infants. He also excluded all infants who at any time had had infection. No such rigid selection was practiced in the present study. All infants were included, both artificially and naturally fed, who were judged by the attending physician to be in good health at the time the blood specimen was taken. Other factors, such as race, climate, altitude, and even differences in method or technique, cannot be excluded as additional possible explanations for the disparity between the hemoglobin levels in the two studies.

The variability in the various factors studied is indicated by the standard deviations. In general, the mean $\pm$ 1 standard deviation constitutes the range within which approximately two-thirds of the values in each age group were found. From Table 3 it is evident that the greatest variability in hemoglobin level occurred in the one-month-old infants. Since the age range of this group is from 1 to 2 months,

3. Elvehjem, C. A.; Peterson, W. H., and Mendenhall, D.: Hemoglobin Content of the Blood of Infants, Am. J. Dis. Child. **46**:105-112, 1933.

4. Mugrage, E. R., and Andresen, M. I.: Values for Red Blood Cells of Average Infants and Children, Am. J. Dis. Child. **51**:775-791, 1936.

5. MacNamara, H., and Senn, M. J. E.: Glutathione and Red Cells in the Blood in Infancy and in Childhood, Am. J. Dis. Child. **59**:97-106, 1940.

6. Mackay, H. M. M.: The Normal Hemoglobin Level During the First Year of Life, Revised Figures, Arch. Dis. Childhood **8**:221-225, 1933.

in the younger infants in this age group the postnatal readjustment in the blood undoubtedly was still proceeding at a rapid rate, whereas in the older infants the blood picture was changing less rapidly. Variations from the mean after the second month of life were only about one-half as great and did not differ significantly from month to month. On the other hand, the variability in erythrocyte counts in the one-month-old infants was no greater than in succeeding months, indicating that postnatal readjustment in the number of cells does not proceed at the same rate as does that of the hemoglobin.

The hemoglobin content of the individual red blood cells was calculated by use of the Wintrobe (1931) [7] formula. As shown in Table 3, the mean corpuscular hemoglobin was highest in the one-month-old infants and decreased with age, the boys showing more extensive decreases in the first five months than the girls. This is in line with the observed sex difference in hemoglobin values which will be discussed later. For the boys at one month of age, the value was 32.5 micromicrograms and for the girls 31.8 micromicrograms. The values diminished rapidly to 26.0 micromicrograms at 5 months of age for the boys, with slightly lower values during the remainder of the first year of life. For the girls, the value at 5 months was 27.8 micromicrograms, with values around 27.0 micromicrograms in most of the succeeding months. Faxén's values were considerably higher than those in the present study, reflecting the disparity in hemoglobin values discussed earlier. These findings suggest that the infants in Faxén's study had red blood cells which were appreciably larger than those of the infants in the present investigation. Measurements of the mean red blood cell diameter of the infants in this study are in progress and will be published at an early date. A comparison of these results with those of Faxén should be of considerable interest, since it is generally agreed that one of the characteristics of hypochromic anemia is a diminution in the size of the red blood cell. If there is evidence that the infants in the present study had some degree of hypochromic anemia, it seems likely that a large percentage of infants under one year old in this country likewise are suffering from this condition.

Hamil and his associates (1938),[8] in a study of the quantitative relations between hemoglobin, erythrocytes, and leucocytes, found that within certain limits the hemoglobin and red cells are independent and that erythrocyte counts have little predictive value as to the hemoglobin level. As a measure of the degree of association beween the red cell counts and the hemoglobin levels in the present study, coefficients of correlation were computed separately on the data for the boys and the girls. The results showed that, although the association between the two factors was highly significant, nevertheless, for the boys only 16.6% ($r^2 \times 100 = 16.65$), and for the girls 12.7%, of the variation in hemoglobin was due to the variation in red cell counts, thus substantiating the findings of Hamil and his associates.

Table 3 shows that, at practically every age, the mean hemoglobin value for the girls exceeded that for the boys. The difference, when tested statistically, was found to be highly significant. This observation is contrary to the observation of

7. Wintrobe, M. M.: The Direct Calculation of the Volume and Hemoglobin Content of the Erythrocyte: A Comparion of Color Index, Volume Index and Saturation Index Determinations, Am. J. Clin. Path. **1**:147-165, 1931.

8. Hamil, B. M.; Poole, M. W.; Munday, B.; Shepherd, M. L.; Emerson, L.; Macy, I. G., and Raiford, T. E.: A Consideration of Quantitative Relations Between Erythrocytes, Leucocytes, and Hemoglobin of the Blood, J. Lab. & Clin. Med. **23**:488-496, 1938.

Elvehjem and his associates, who secured practically identical values for the boy and girl infants in their study. Downey (1938) [9] stated that birth weight and rate of growth have a decided influence on the hemoglobin level in the first year of life. Washburn (1941) [10] concluded from weekly observations on 15 infants that the decrease in red blood cells, hemoglobin, and packed cell volume in the first 6 to 9 weeks of life is dependent largely on two factors: (1) the rapid increase in total body mass and (2) the abrupt decrease in reticulocytes, indicating a sudden decrease in the rate of production of red cells.

To ascertain whether the higher hemoglobin values for the girls in the present study were attributable to smaller birth sizes, less rapid growth, or both, birth weight and body weight at the time the blood samples were secured were tabulated for each infant. From these data the gain in weight from birth was computed. In Table 4 are given the means of birth weights, weight gains, and hemoglobin

TABLE 4.—*Hemoglobin Values for Boy and Girl Infants from Two St. Paul Well-Baby Clinics in Relation to Birth Weight and Gain in Weight from Birth*

	Boys				Girls			
Age, Mo.	Observations, No.	Birth Weight, Oz.	Gain in Weight from Birth, Oz.	Hemoglobin, Gm./100 Ml.	Observations, No.	Birth Weight, Oz.	Gain in Weight from Birth, Oz.	Hemoglobin, Gm./100 Ml.
1- 2	22	118	45	12.33	15	122	38	12.99
2- 3	25	121	82	11.25	20	118	69	11.51
3- 4	17	118	106	11.72	15	122	97	12.24
4- 5	20	117	132	12.36	11	118	108	12.76
5- 6	13	123	144	12.36	15	120	135	12.56
6- 7	10	109	178	11.97	8	116	140	12.20
7- 8	11	123	181	11.99	6	119	149	11.94
8- 9	9	112	194	11.74	10	115	174	12.21
9-10	3	122	199	11.98	9	125	213	12.29
10-11	4	124	210	11.87	6	114	183	12.18
11-12	7	120	210	11.77	6	122	219	12.27
12-13	3	108	240	12.07	2	110	226	11.70

levels for the infants in each age group. These values are based on the data secured in 1949-1950 at the two St. Paul clinics. The Minneapolis data were not included because the infants usually were not weighed on the same day that the blood specimen was taken. These data show that there was little difference in the mean birth weight of the sexes. In some age groups the girls and, in others the boys, had the higher mean birth weight. On the other hand, in practically every age group the boys showed the greatest gain in weight from birth. This would seem to indicate that in the present series the lower hemoblobin levels of the boys were due to their more rapid growth, with failure of hemoglobin production to keep up with the rapidly expanding blood volume.

Kato and Emery (1933) [11] emphasized the fact that many factors influence the hemoglobin level in infancy, including, season of the year, state of nutrition, and infections. Mackay (1931) [1] found that in a group of artificially fed infants the

9. Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, Vol. 2.

10. Washburn, A. H.: Blood Cells in Healthy Young Infants: Postnatal Readjustment of the Red Blood Cells in Individual Babies, Am. J. Dis. Child. **62**:530-544, 1941.

11. Kato, K., and Emery, O. J.: Hemoglobin Content of the Blood in Infancy, Folia haemat. **49**:106, 1933.

frequency of infectious diseases was twice as great in untreated children as in those children who had been treated with iron compounds. Faxén pointed out that infectious diseases occur most frequently during the dark season of the year and suggested that they undoubtedly play an important role in determining the hemoglobin level. He found little or no evidence of seasonal variation in the hemoglobin level of the infants in his study and considered this suggestive evidence that the lower hemoglobin levels noted by other workers during the winter months were due to the greater incidence of infections at this season of the year. It will be recalled that Faxén included in his study only those infants who, as far as was known, had had no infections of any kind.

To test whether there was evidence of seasonal variation in hemoglobin level in the present study, the data for the 3-, 4-, 5-, and 6-month-old infants were divided into two series: (1) those which were obtained in the six months from the first of June to the end of November, and (2) those secured in the remaining six months of the year. This division was selected as representing the months of more and less favorable weather in Minnesota. Furthermore, Platt and Freeman (1930)[12] had observed lower hemoglobin values in February than in November and suggested that the peak probably came in summer. The results of this tabulation

TABLE 5.—*Seasonal Variation in Hemoglobin Level in Young Infants*

	Boys				Girls			
	June to Nov.		Dec. to May		June to Nov.		Dec. to May	
Age, Mo.	Cases, No.	Hemoglobin, Gm./100 Ml.	Cases, No.	Hemoglobin, Gm./100 Ml.	Cases, No.	Hemoglobin, Gm./100 Ml.	Cases, No.	Hemoglobin, Gm./100 Ml.
3-4	13	12.04	17	11.93	11	12.23	19	12.10
4-5	16	12.27	16	12.02	11	12.66	14	12.56
5-6	15	12.22	15	12.23	13	12.68	11	12.66
6-7	14	11.65	10	12.08	7	12.09	11	12.35

are given in Table 5. This shows that for the 3- and 4-month-old infants the mean hemoglobin values for the summer months were slightly higher than those for the winter months, but the differences were not significant. On the other hand, there is no difference between the values for the two seasons in the 5-month-old infants, and in the 6-month-old groups the mean values for the winter season are actually higher than in the summer season. To demonstrate the possible significance of such small differences, as pointed out earlier, would require the accumulation of a much larger volume of data than was obtained in the present study.

SUMMARY

The present study included 267 infants, ranging in age from 1 to 12 months, on whom were made 517 estimations of the amount of hemoglobin and the number of red blood corpuscles. The infants were studied at three well-baby clinics in Minneapolis and St. Paul and were judged to be in good health at the time the blood specimens were taken.

The mean hemoglobin level, which was approximately 12.50 gm. per 100 ml. of blood in the 1-month-old infants, decreased sharply and reached a minimum of

12. Platt, V. E., and Freeman, R. G.: Seasonal Variation in Hemoglobin, Proc. Soc. Exper. Biol. & Med. **27**:687-688, 1930.

11.35 gm. in the 2-month-old infants. The hemoglobin level showed a recovery in the succeeding three months to 12.45 gm., followed by a second moderate decline and a gradual recovery in the second half of the year. In practically every age group the hemoglobin level of the boys was somewhat lower than that of the girls. This difference appeared to be due to the more rapid growth of the boys, with apparent inability of hemoglobin production to keep up with the rapidly expanding blood volume.

The number of red blood corpuscles in the one-month-old infants was about 4,000,000 per cubic millimeter of blood. The number decreased to 3,800,000 in the 2-month-old infants and thereafter showed a gradual recovery to about 4,900,000 by the end of the first year of life.

The mean hemoglobin content of the individual cells was high, approximately 32.0 micromicrograms in the one-month-old infants, decreased rapidly to about 27.0 micromicrograms during the next several months, and decreased more slowly thereafter. In the boys, in keeping with their lower hemoglobin levels, the mean corpuscular hemoglobin level decreased more rapidly than in the girls, and it remained at a lower level throughout the first year of life.

No evidence of seasonal variation in hemoglobin level was demonstrated by the data secured in this study, although slightly lower values were secured in the 3- and 4-month-old infants during the colder months than during the warmer months. This seasonal difference was not observed in the 5- and 6-month-old infants.

SPINA BIFIDA

Survey of Two Hundred Twenty-Five Encephaloceles, Meningoceles, and Myelomeningoceles

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CONGENITAL anomalies, formerly of chiefly academic interest, are now justifying increased attention. Every physician during his practice may encounter several patients whose conditions may be ameliorated or cured by judicious care or surgical intervention. Spina bifida, with its related neurologic anomalies, has been a source of perplexity for many years to the general practitioner, pediatrist, neurologist, and surgeon. Even when a case appears to be hopeless, however, a competent understanding of these lesions and their clinical manifestations permits the physician to answer intelligently the questions posed by anxious parents and to instruct them in treatment and prognosis. Ingraham's [1] comprehensive bibliography sets forth more than 2,000 references on the subject, most of which consist of reports of one or a few cases. It is the purpose of this discussion to present a survey of 225 encephaloceles, meningoceles, and myelomeningoceles studied in the University Hospitals during the period from 1938 to 1950.

ETIOLOGY

The causative factor or factors of these spinal and neural malformations is not known. Mall [2] narrated certain beliefs held in the past that they were due to supernatural causes, hybrids of bestial origin, and maternal impressions. He contended that they were the result of adverse external influences playing upon normal ova and giving rise to nutritional disturbances of faultily implanted embryos. In Campbell's [3] review of the relevant embryology, it is stated that fusion of the neural tube occurs between the 21st and 29th day after ovulation. Mesenchyma, derived from the mesoderm of the supporting somites, is necessary to stimulate this integrated movement. Myelomeningoceles and encephaloceles accompanying spina bifida and cranium bifidum may be construed as arising from faulty induction of ectoderm secondary to mesenchymal defects. The cause of the protean forms of spina bifida and accompanying vascular, fatty, and meningeal defects may reasonably

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Lloyd A. Knowler, Professor and Chairman of the Department of Mathematics and Astronomy, State University of Iowa, and Mr. James B. Bartoo assisted in the preparation of the statistical data.

1. Ingraham, F. D.: Spina Bifida and Cranium Bifidum, Cambridge, Mass., Harvard University Press, 1944, pp. 1-216.

2. Mall, F. P.: A Study of the Causes Underlying the Origin of Human Monsters, J. Morphol. **19**:3-368, 1908.

3. Campbell, J. B.: Congenital Anomalies of the Neural Axis: Surgical Management Based on Embryologic Considerations, Am. J. Surg. **75**:231-256, 1948.

be ascribed to the mutipotential nature of mesenchyma, a primitive tissue which gives rise to fat, fascia, muscle, blood vessels, components of the vertebral column, notochord, chondral and membranous portions of the skull, and some portions of the meninges. Whether these variations are the result of adverse genetic factors, alterations of the environment of the uterus, or both is far from settled.

CLASSIFICATION

According to Frazier [4] the term spina bifida was introduced by Nicolai Tulpius about the middle of the seventeenth century. Etymologically rachischisis (Greek) and spina bifida (Latin) are synonymous, both referring to a cleft in the vertebral column. Lichtenstein's [5] designation, dysraphism (spinal or cranial), is perhaps a preferable generic term, since rachischisis has been employed to denote a complete nonunion of the walls of the medullary canal, following von Recklinghausen's [6] monograph in 1886.

Spina bifida occulta refers to incomplete closure of the vertebral laminae, which may be demonstrated upon roentgenologic examination. It is occasionally associated with enuresis, incontinence, maldevelopment of the feet or lower extremities, or other local abnormality, such as scoliosis, hypertrichosis, or a lipomatous mass. The appearance of symptoms is often delayed until the second decade of life.

The following conditions are sometimes referred to as spina bifida cystica or manifesta.

Rachischisis is an extreme spina bifida with wide bony defect due to absence of laminae and pedicles. There is little or no sac formation. The nervous tissue is directly exposed.

The term spina bifida with meningocele is reserved for conditions in which a sac of dura mater or of dura mater and arachnoid protrudes through a cleft in the vertebrae. Nerve elements are not visible, and there is no evidence of neurologic disability. The collection of fluid may be in the subdural or subarachnoid space posterior to the cord or cauda equina.

The term spina bifida with myelomeningocele refers to a cystic protrusion with contained nerve elements and is often characterized by muscular weakness, loss of sphincter tone, and/or disturbances in cutaneous sensation.

Frazier [4] emphasized the frequent occurrence of solid tumor, most often a lipoma, with these defects. Ingraham and Swan,[7] impressed by the association of these anomalies with an overgrowth of fatty tissue, employ the term lipoma if such a tumor is present with spina bifida occulta and lipomeningocele when associated with a meningeal sac. If nerve elements are also involved, they suggest the term lipomyelomeningocele.

Syringomyelocele or myelocystocele is a protrusion of membranes and cord, but the fluid is in the dilated central canal.[8]

4. Frazier, C. H.: Surgery of the Spine and Spinal Cord, D. Appleton & Company, New York, 1918, pp. 265-324.

5. Lichtenstein, B. W.: "Spinal Dysraphism"; Spina Bifida and Myelodysplasia, Arch. Neurol. & Psychiat. **44**:792-810, 1940.

6. von Recklinghausen, F. D.: Untersuchungen über die Spina bifida, Virchows Arch. path. Anat. **105**:243, 1886.

7. Ingraham, F. D., and Swan, H.: Spina Bifida and Cranium Bifidum (Encephalocele): Survey of 546 Cases, New England J. Med. **228**:559-563, 1943.

8. Turnbull, F. A.: Syringomyelic Complications of Spina Bifida, Brain **56**:304-317, 1933.

In rare instances, meningocele may extend anteriorly into the sacrum or through vertebral bodies or the intervertebral foramina into the thorax or lumbar region.[9]

Encephalocele is a general term to describe herniation of the meninges or brain tissue through a defect in the cranium. Basal varieties, relatively rare, may extend into the nose, pharynx, or orbit. Sincipital types present as external tumors. The terms cranium bifidum with meningocele and cranium bifidum with encephalomeningocele may be used to distinguish between a simple cyst and one in which brain tissue is included. Cranioschisis refers to a condition in which brain tissue is exposed and little or no sac exists.

The present report is restricted to 26 (11.5%) encephaloceles and 199 (88.5%) meningoceles studied in University Hospitals in the 12-year period beginning in 1938. Information from the hospital records was supplemented by a 50-item questionnaire which was sent to the parents. One hundred sixty-seven (74%) questionnaires were completed and returned.

TABLE 1.—*Incidence of Spina Bifida, Meningocele, Myelomeningocele, and Encephalocele, in Live Births in Iowa, 1941-1949*

Year	Live Births, No.	Anomalies, No.	Incidence per 10,000
1941	46,825	59	12.6
1942	49,235	44	8.9
1943	48,209	26	5.3
1944	46,914	40	8.5
1945	45,265	31	6.8
1946	57,202	39	6.8
1947	64,975	49	7.5
1948	61,506	65	10.5
1949	62,897	71	11.2
Total	483,028	424	Average 8.7

INCIDENCE

In this series there were 225 encephaloceles, meningoceles, and myelomeningoceles among 257,295 hospital admissions, an incidence of 1 in 1,143 or 87 in 100,000. Ingraham and Swan [7] report a ratio of 1 to 4,150 new admissions. Economic levels seem proportional to the total number of patients in each classification. With the exception of one Negro and one Mexican, all patients were of European stock.

Mall,[2] from studies of pathological embryos, estimated that there would be one fetus with spina bifida in 1,000 pregnancies. In University Hospitals in the 24 years from 1926 to 1949 there were 22,175 births with 32 instances of anomalies of the spine classified as spina bifida manifesta, an incidence of 14.5 in 10,000. Table 1 records the incidence of meningocele, myelomeningocele, and encephalocele in live births in Iowa for nine years, 1941-1949. The average is 8.7 in 10,000. Murphy [10] states that the birth rate of defective persons in the general population is 47 in 10,000 live births. Among deceased but live-born, the rate climbs to 54 in 10,000, and among stillborn infants 297 in 10,000 possess congenital malformations. Therefore malformations are observed in stillborn infants nearly 5.5 times

9. (*a*) Eder, D.: Anterior Sacral Meningocele: Survey of Literature and Report of a Case, Bull. Los Angeles Neurol. Soc. **14**:104-112, 1949. (*b*) Pendergrass, R. C.; Walker, A. E., and Bond, J. P.: Extraspinal Lumbar Meningocele, J. Neurosurg. **4**:80-86, 1947.

10. Murphy, D. P.: Congenital Malformations, Ed. 2, Philadelphia, J. B. Lippincott Company, 1947.

as often as in the live-born. It would seem that Mall's [2] forecast in 1908 from examination of pathological embryos bears a close approximation to our clinical findings.

SEX

In this series there were 139 (61.8%) females and 86 (38.2%) males. When examined statistically this proved to be highly significant. If we assume the occurrences were equally likely among males and females, the frequency of occurrence in males would fall in the range 90 to 135, on an average of 99.7% of the times. In the present study the figure 86 (males) falls outside the above interval, which tends to indicate that our assumption of "equally likely" is false. Hence we may assume that the incidence of this anomaly is higher among females. In Ingraham and Swan's [7] series there were 296 females and 250 males. The series

TABLE 2.—*Age of Patient When First Admitted*

Age	No.	Per Cent
Less than 1 wk.	32	14.2
1- 3 wk.	31	13.8
1-11 mo.	122	54.2
12-23 mo.	14	6.2
2- 4 yr.	6	2.7
5-11 yr.	10	4.5
12-19 yr.	4	1.8
20-39 yr.	1	.4
40-58 yr.	5	2.2
Total.	225	100.0

TABLE 3.—*Location of Lesion*

Location	No.	Per Cent
Cranial (11.5%)		
Frontal	7	27.
Occipital	19	73.
Total	26	100.
Spinal (88.5%)		
Cervical	2	1.0
Thoracic	9	4.5
Thoracolumbar	25	12.6
Lumbar	105	52.8
Lumbosacral	37	18.6
Sacral	18	9.0
Not located	3	1.5
Total	199	100.0

of 84 cases reported by Siris [11] was the only report encountered in which there were more males than females (46 to 38). In the 45 verified examples of anterior sacral meningocele which Eder [9a] collected from the literature, only 6 cases occurred in males. The sex was not specified for two infants.

AGE

Twenty-eight per cent of the patients were brought for examination in the first three weeks of life and 82.2% in the first year (Table 2). The average age of the 215 children was 7 months and of the 10 adults was 31 years.

LOCATION

Table 3 records the site in which these lesions were found. The preponderance of meningoceles and myelomeningoceles in the lumbar region agrees with the

11. Siris, I. E.: Spina Bifida: Treatment and Analysis of 84 Cases, Ann. Surg. **103**:97-123, 1936.

findings of other writers.[12] In none of the patients in this series were multiple lesions discovered. Occipital encephaloceles are more frequently encountered than those in the vertex or frontal region.

DESCRIPTION OF LESION

The nature of the covering of the sac is listed in Table 4. Normal skin was recorded in 45 cases (20%). In 21 cases (9.3%) there was a dimpling of the covering of the cyst which has been referred to as an "umbilicus." In 143 records the examiner had recorded a measurement of the longitudinal and transverse diameters, with an average of 6.7 and 6.0 cm., respectively. In 62 cases the elevation was noted, and these figures average 3.4 cm. The mass was growing in 88 of 151 cases (58.3%), and there was a history of drainage in 113 of 190 cases (59.5%). Telangiectasis and hair were present in 20% of cases.

CONTENTS OF THE CYST

Lichtenstein [13] has outlined in detail the cutaneous, the mesodermal, and the neural defects of spinal dysraphism. The contents of the sac were adequately described in 109 cases of the present series. In 90 patients (82.6%) there were

TABLE 4.—*Description of Cystic Lesion*

	No.	Per Cent
Ulcerating, granulating	46	20.5
Transparent, parchment, embryonal skin	86	38.2
Furrowed, scarred, lobulated	22	9.8
Normal skin	45	20.0
Unsatisfactory or no description	23	10.2
Canal open (rachischisis)	3	1.3
Total	225	100.0

nerve roots or spinal cord or brain tissue. Of the 26 encephaloceles, 15 contained brain tissue, in 5 cases it was reported absent, and in 6 this information was not obtained. Three dermoids, one hemangioma, and two teratomas were encountered. The latter are benign growths, but one of the competent tissues may undergo cancerous degeneration.[14] This occurred in a 5-year-old girl with spina bifida and a meningocele which had not been operated upon. She entered the hospital with signs of recent rapid increase in growth of the cyst, simulating infection, paresis of the lower limbs, and paralysis of bowel and bladder function. A sarcoma was identified. Metastases to the lungs developed and the child died four months after the onset of symptoms. The prevention of this tragic, although rare, complication constitutes one reason for exploration and repair of these cystic lesions, even if they are asymptomatic.

INCIDENCE OF MYELOMENINGOCELE

Most authors agree that about 75% of patients with manifest spina bifida will have myelomeningoceles: Ingraham and Swan,[7] 409 cases (72.6%); Siris,[11] 84

12. Moore, J. E.: Spina Bifida with Report of 385 Cases Treated by Excision, Surg. Gynec. & Obst. **1**:137, 1905. Siris.[11] Ingraham and Swan.[7]

13. Lichtenstein, B. W.: Distant Neuroanatomic Complications of Spina Bifida (Spinal Dysraphism), Arch. Neurol. & Psychiat. **47**:195-214, 1942.

14. DeVeer, J. A., and Browder, J.: Sacrococcygeal Teratoma, Ann. Surg. **105**:408-417, 1937.

cases (77.4%). In this series of 199 patients with spinal dysraphism there were 146 with weakness or paralysis of the lower limbs, an incidence of myelomeningocele of 73.4%.

GENITOURINARY AND BOWEL DISTURBANCES

Paralysis of bowel and bladder was recorded in 117 cases (58.8%). These complications, difficult to assess in the infant, are less reliable findings than muscular weakness in distinguishing a meningocele from a myelomeningocele. The problem of spina bifida and urinary incontinence has been investigated and reported upon by McCarroll [15] and by Langworthy and Dees.[16] Prolapse of the rectum was noted in 23 instances, or 11.6% of cases with the spinal abnormality. Torpin [17] has reported upon prolapse of the uterus associated with spina bifida, but this condition was not recorded in any cases in this series. Decubitus or trophic ulcers, more frequently encountered in adults, were present in 15 cases, or 6.7%.

TABLE 5.—*Two Hundred Seventeen Associated Abnormalities in 100 Cases (Excluding Club Foot, Dislocated Hip, and Hydrocephalus)*

Bones	
Femur	4
Exostosis	1
Vertebral	15
Ribs	7
Skull	5
Lückenschädel	12
Sprengel's deformity	1
Kyphoscoliosis	10
Central Nervous System	
Microgyria	3
Porencephaly	1
Cerebellum	1
Arnold-Chiari malformation	16
Stenosis aqueduct	2
Hydromyelia	7
Absent cervical roots	1
Constricting cervical band	1
Deaf-mutism	3
Heart	5
Pilonidal	37
Face	
Mongoloid facies	4
Deformed nose	2
High palate	2
Hypertelorism	4
Strabismus	18
Spherophakia	1
Malocclusion	1
Genitourinary System	
Double kidney	3
Extrophy	1
Hydrocele	4
Small genitalia	2
Undescended testes	7
Cystic kidney	1
Miscellaneous	
Hernia	7
Nipples supernumerary	1
Digits	11
Pyloric stenosis	1
Absent large bowel	1
Rectovaginal fistula	1
Imperforate anus	1
Stridor	1
Neurofibromatosis	2
Speech defect	5
Conjoined twins	1
Hemangioma face	2
Teratoma	3

ASSOCIATED CONGENITAL ANOMALIES

The frequency with which spina bifida is associated with other congenital anomalies is noteworthy. Ingraham and Swan [7] reported 570 associated anomalies in 232 patients, slightly more than half the series. They included club feet, dislocated hips, and hydrocephalus, which may have been secondary to the spinal cord or caudal lesions. In the present series, the 217 associated abnormalities (excluding club feet, dislocated hips, and hydrocephalus) present in 100 cases are summarized in Table 5. No other abnormality except the primary lesion (menin-

15. McCarroll, H. R.: Spina Bifida Urinary Incontinence: A Report of Cystometric Studies in a Series of 30 Cases, Surg. Gynec. & Obst. **64**:721-737, 1937.

16. Langworthy, O. R., and Dees, J. E.: A Study of Bladder Disturbances in Spina Bifida, J. Urol. **35**:213-226, 1936.

17. Torpin, R.: Prolapsus Uteri Associated with Spina Bifida and Club Feet in New Born Infants, Am. J. Dis. Child. **66**:627-628, 1943.

gocele, myelomeningocele, or encephalocele) was found in 45 cases (20%). The "cranial" group exhibited associated malformations slightly more frequently than the "spinal" group.

In Table 6 are recorded the number of cases and percentage incidence of club foot (40.9%), dislocated hip (5.8%), and hydrocephalus (52.0%). These are somewhat higher than the figures reported by Ingraham and Swan [7] (clubfoot, 18%; dislocated hip, 4%; hydrocephalus, 36.5%). They point out that the records in these items are probably incomplete.

ARNOLD-CHIARI MALFORMATION

Russell and Donald [18] offered a mechanical explanation for the production of communicating hydrocephalus in a series of myelomeningoceles, holding that "the plugging of the upper cervical canal by the Arnold-Chiari malformation hinders

TABLE 6.—*Incidence of Club Foot, Dislocated Hip, and Hydrocephalus*

Abnormality	No.	Per Cent
Club foot		
Bilateral	63	28.0
Unilateral	21	9.3
Other foot deformity	8	3.6
None	81	36.0
Unknown	52	23.1
Total	225	100.0
Dislocated hip		
Bilateral	11	4.9
Unilateral	2	0.9
Total	13	5.8
Hydrocephalus		
Present	117	52.0
Absent	91	40.5
Unknown	17	7.5
Total	225	100.0

upward flow into the subarachnoid channels of the posterior fossa." A high proportion of infants with myelomeningocele may be expected to harbor a coexisting Arnold-Chiari malformation. Gordon,[19] in a series of 14 autopsies on patients with myelomeningocele, reported that 13 had hydrocephalus, of which 8 proved to have Arnold-Chiari malformation. Russell and Donald [18] reported the malformation in 10 consecutive cases of myelomeningocele, 8 of which presented hydrocephalus. On the other hand, Lichtenstein [13] believed that stenosis of the aqueduct accounts for more cases of hydrocephalus associated with Arnold-Chiari malformation than does interference with the flow of cerebrospinal fluid at the level of the foramen magnum. He reported three cases with spina bifida, Arnold-Chiari malformation, stenosis of the aqueduct, and hydrocephalus. Shryock [20] presented a case with a

18. Russell, D. S., and Donald, C.: The Mechanism of Internal Hydrocephalus in Spina Bifida, Brain **58**:203-215, 1935.

19. Gordon, W.: Meningocele and Myelomeningocele, M. Press **221**:566-569, 1949.

20. Shryock, E. H.: Complete Obstruction of the Cerebral Aqueduct Associated with Lumbar Meningocele, Bull. Los Angeles Neurol. Soc. **9**:163-166, 1944.

completely obstructed aqueduct. Ingraham and Scott [21] have reviewed the literature on the Arnold-Chiari malformation and make the observation that as more autopsy material is available more such anomalies will be discovered. In their series, only 20 cases of Arnold-Chiari malformation are listed. In the present series there were but 16 proved cases. Autopsy was performed for only 32 (37.2%) of the 86 patients known to have died.

PILONIDAL SINUS OR DIMPLE

Mallory [22] studied 19 cases of pilonidal sinus and concluded that the lesion arose in the remnants of the normally obliterated medullary canal. Gage [23] agreed with this but concluded that coccygeal dimples result from disturbances in development of the coccygeal ligament and are not connected with the medullary canal. Hamby [24] reported a case with familial incidence of pilonidal cyst and spinal dysraphism. Walker and Bucy [25] have called attention to congenital dermal sinuses as a source of spinal meningeal infection and subdural abscess. Ingraham and Swan [7] reported 13 cases of pilonidal sinus in 570 patients (2.3%). In the present series of 225 cases, pilonidal sinuses or dimples were recorded in 37 patients (16.5%).

TREATMENT

The child with spina bifida is frequently referred for consultation early because of the apprehension of the attending physician and of the parents that the distended, thin-walled cyst may rupture. Symptoms from these lesions are ascribable to (1) the presence of the cystic tumor, with the constant threat of rupture, sepsis, and meningitis; (2) neurological dysfunction due to involvement of the spinal cord, cauda equina, or nerve roots, and (3) associated malformations and defects, including disturbances in cerebrospinal-fluid circulation.

Repair is undertaken in selected cases to attempt to prevent accidental rupture and meningitis, for cosmetic purposes, to facilitate the care of the infant, to preclude cancerous degeneration in teratomatous tissue, and to free the cord and cauda equina from interference with its normal "migration" up the spinal canal. Surgical intervention is not advised in cases in which severe neurological deficits are present, such as total or near-total paralysis of bowel and bladder function and paraplegia.

The subject of conservative, symptomatic, and surgical therapy of these lesions has received extensive consideration by several authors.[26] Frazier,[4] Ingraham and

21. Ingraham, F. D., and Scott, H. W., Jr.: Spina Bifida and Cranium Bifidum, Arnold-Chiari Malformation: Study of 20 Cases, New England J. Med. **229**:108-114, 1943.

22. Mallory, F. B.: Sacro-Coccygeal Dimples, Sinuses and Cysts, Am. J. M. Sc. **103**:263, 1892.

23. Gage, M.: Pilonidal Sinus, Arch. Surg. **31**:175-189, 1935.

24. Hamby, W. B.: Pilonidal Cyst, Spina Bifida Occulta and Bifid Spinal Cord: Report of a Case with Review of the Literature, Arch. Path. **21**:831-838, 1936.

25. Walker, A. E., and Bucy, P. C.: Congenital Dermal Sinuses: A Source of Spinal Meningeal Infection and Subdural Abscesses, Brain **57**:401-421, 1934.

26. (*a*) Frazier.[4] (*b*) Penfield, W., and Cone, W.: Spina Bifida and Cranium Bifidum: Results of Plastic Repair of Meningocele and Myelomeningocele by a New Method, J. A. M. A. **98**:454-461, 1932. (*c*) Hyndman, O. R.: Visible Congenital Maldevelopments of Neurosurgical Character About the Head and Spine, J. Iowa M. Soc. **33**:158-166, 1943. (*d*) Gross, S. W., and Sachs, E.: Spina Bifida and Cranium Bifidum: A Study of 103 Cases, Arch. Surg. **28**:874-888, 1934. (*e*) Siris.[11]

Hamlin,[27] and Chambers [28] have especially clear and well-illustrated accounts of the excision of the cyst and the plastic repair. Pinheiro [29] believed that the cystic bag should be immediately protected by a full-thickness skin graft and that operation should be postponed until after the fourth year.

The age at which repair is undertaken depends to some extent on the fragility of the cyst wall. A few are so deficient that the lesion must be dealt with within the first 24 hours of life. The infant should be examined early in order that the surgeon may make a careful evaluation of neurological status and recommend a program to promote epithelization and control of infection. The oozing, granulating, distended cyst is treated with bland ointments and protected with a large circumferential dressing or "doughnut" when the child is transported or must lie on his back or his side. The infant is best maintained on a Bradford frame in the prone position, with the lesion exposed and dry or alternately treated with boric acid soaks or applications of baby oil, depending upon the appearance of the covering of the sac. Orthopedic care should be instituted early for the prevention and active treatment of deformities of the extremities. Such a period of conservative home care permits the infant to mature and thus to be better prepared for surgery. It also affords the surgeon a period of temporization in which to appraise the infant neurologically during the early period of rapid growth and development. In this period of observation the hydrocephalus may become self-arrested. Frazier's [4] practice was to postpone surgery until after the first year "when the unfit are sifted out." With the renewed interest in shunting of cerebrospinal fluid into the ureter [30] and treatment of hydrocephalus by ventriculomastoidostomy,[31] it may be expedient in selected cases to deal with the hydrocephalus before surgical attention is directed at the sac.

In Ingraham and Swan's [7] series, 208 patients (52%) were considered suitable for operation. Siris,[11] with 84 patients, operated upon 37 (44%). Gross and Sachs [26d] carried out surgery on 57 of 103 patients (55%). In this series 21 encephaloceles (80.7%) were operated upon, and 78 (39.2%) of the patients in the spinal group came to surgery. The combined surgical group was 99 of 225 patients (44%).

The essential features of the actual operation consist of excision of the sac, with preservation of maximal spinal-cord tissue and nerve roots; reconstruction of the dural tube; reinforcement with imbricated flaps of lumbodorsal fascia; mobilization of the skin, and plastic closure aimed at reducing tension on the wound edges. The wound is dressed in such a way as to prevent fecal and urinary contamination, and the infant is maintained in the prone position on a Bradford frame, with the head lowered to reduce the subarachnoid-fluid pressure at the operation site. Excretory cleanliness must be rigorously maintained. When the

27. Ingraham, F. D., and Hamlin, H.: Spina Bifida and Cranium Bifidum (Encephalocele): Surgical Treatment, New England J. Med. **228**:631-641, 1943.

28. Chambers, W. R.: Technique for the Early Operation of Myelocele and Meningomyelocele, Am. J. Surg. **80**:386-393, 1950.

29. Pinheiro, O. C.: Skin Graft for Spina Bifida with Meningocele or Myelomeningocele, J. Internat. Coll. Surgeons **3**:438-440, 1940.

30. Matson, D. D.: A New Operation for the Treatment of Communicating Hydrocephalus, J. Neurosurg. **6**:238-247, 1949.

31. Nosik, W. A.: Treatment of Hydrocephalus by Ventriculomastoidostomy, J. Pediat. **37**:190-194, 1950.

cerebrospinal-fluid pressure is not controlled by gravity or periodic aspiration, a system of constant lumbar drainage may be instituted.[32]

Until the past two decades surgeons were frequently concerned with effecting an osteoplastic closure of the spina bifida. At present scant attention is given to the bony defect. Recently Scoville and McLaurin [33] have proposed that tantalum mesh be used as a means of plastic repair. Penfield and Cone,[26b] convinced that considerable absorption of cerebrospinal fluid takes place within the sac, recommend preserving and rolling the membranes and constructing a fascial tent over them.

MORTALITY

Moore [12] collected all the reports of treatment by excision he could find in the Surgeon General's library up to 1905 and estimated an operative mortality at 50%. In 1917 Harmer [34] reported a 40% mortality in 34 cases, and in 1924 Cutler,[35] in 62 cases at the Children's Hospital in Boston, reported a 60% mortality. Kolodny [36] in 1933 claimed a mortality of 5% in 60 cases. Gross and Sachs [26d] in 1934 reported upon 57 patients with a mortality of 27%. Siris [11] in 1936 reported 32.3% mortality in 37 operations. Ingraham and Swan [7] in 1943 reported a 12% mortality in 188 cases. In the present series of 78 patients operated upon for meningocele and myelomeningocele, the operative mortality was 8%. These occurred on the 32d, 30th, 29th, 21st, and 4th postoperative days, as a result of meningitis. One patient with a teratoma is listed as having died of shock in the operating room. There were no deaths following repair in the encephalocele group. Two of these patients, repaired in childhood, died at the ages of 9 and 19 years. These deaths followed ventriculography which had been performed to investigate progressive hydrocephalus and convulsions.

RESULTS

The cases have been evaluated by dividing them into three categories. "Well" indicates a good result, with the child being considered "normal" by the parents. He is able to go to school, carry papers, ride a bicycle, roller skate, and participate in sports and Cub Scout activities. In the group designated "fair" the patient is ambulatory, but there may be muscular weakness, scoliosis, enuresis, or braces. In the third class, "poor," are patients who have vesical and rectal incontinence, with paralysis confining them to chair or bed. Table 7 records the results in spinal and cranial cases, with an estimate of mental status.

In the spinal group of 199 patients, 19.6% are leading useful happy lives, 41.7% have died, 15.5% are paraplegic, and the condition of 23.1% is unknown. Of the 76 patients who survived, 16, or 21%, are considered normal, and 23, or 30%, are suffering from mild neurologic disability. Thirty-seven, or 49%, suffer severe neurologic disability. These figures seem to agree with the estimate made

32. Ingraham, F. D., and Campbell, J. B.: An Apparatus for Closed Drainage of the Ventricular System, Ann. Surg. **114**:1096-1098, 1941.

33. Scoville, W. B., and McLaurin, R. L.: Tantalum Mesh in Repair of Congenital Bony Defects of Skull and Spine, J. A. M. A. **147**:639-640, 1951.

34. Harmer, T. W.: Spina Bifida and Allied Malformations: Based on Operative Experience of 34 Cases, Boston M. & S. J. **177**:353-357, 1917.

35. Cutler, G. D.: End Results in 62 Cases of Spina Bifida and Cephalocele, Arch. Neurol. & Psychiat. **12**:149, 1924.

36. Kolodny, A.: Results of Surgery in Spina Bifida, J. A. M. A. **101**:1626-1630, 1933.

by Ingraham and Swan [7] that about 30% of their patients with spina bifida (including spina bifida occulta) may look forward to a life unhampered by any significant incapacity resulting from their anomaly. In their spinal series, 60 patients were normal, 61 had mild neurologic disability, and 113 had severe neurologic disability.

In the cranial group of 26 patients, 7 (27%) are "well," and 4 (15%) are "fair." Two are in the "poor" classification, 3 have died, and the present status of

TABLE 7.—*Present Status of Spinal and Cranial Groups*

Classification	Total	Mental Status		
		Intelligent	Unknown	Retarded
Spinal Group				
Well	16	16	..	..
Fair	23	20	2	1
Poor	31	21	7	3
Alive, classification unknown	6	..	..	..
Total alive	76	..	..	..
Total dead	83	..	..	..
Total unknown	40	..	..	..
Total	199	..	..	..
Cranial Group				
Well	7	6	1	..
Fair	4	1	..	3
Poor	2	..	..	2
Total alive	13	..	..	..
Total dead	3	..	..	..
Total unknown	13	..	..	..
Total	26	..	..	..

TABLE 8.—*Causes of Death in the Spinal Group*

Diagnosis	No.
Meningitis	
Postoperative	5
Nonoperative	28
Hydrocephalus	9
Convulsions	5
Pneumonia	5
Urinary complications	3
Stillborn	3
Rupture of sac	3
Postplexectomy	3
Prematurity	2
Suboccipital exploration	2
Multiple anomalies	1
Diarrhea	1
Malignant neoplasm	1
Unknown	12
Total	83

13 is unknown. It is no doubt significant to note in Table 7 that only 4 of the 76 infants in the spinal group are classified as mentally retarded, whereas 5 of 13 in the cranial series were so classified. In the 84 cases of encephalocele reported by Ingraham and Swan,[7] 59 had adequate follow-up studies, and 21 (34%) of these, or 25% of the total, were classified as entirely normal. Again, our figures would support their estimate that about one-third of the patients with encephalocele, with the aid of operative therapy, may look forward to a relatively normal existence.

In Table 8 are listed the causes of death in the spinal group. Meningitis accounted for 33 deaths, or 39.75%, and hydrocephalus was responsible for 9, or 10.84%. The average age of the children who died was 12.8 months.

In 1908, Frazier [4] wrote, "Eighty to ninety percent die during the first year and of the small percentage remaining the majority are mentally defective and physically crippled." It seems that this estimate regarding mental status must now be revised. Table 9 reveals that in the present series, 67 (33.6%) of 199 patients died by the time they were one year old. Of the 83 in the fatal spinal group, 80.8% die by the time they are one year old.

COMPARISON OF RESULTS WITH AND WITHOUT SURGERY

Surgical procedures aimed at treating hydrocephalus and Arnold-Chiari malformation to enhance infants' chances for survival have been discussed. It is, however, a difficult task to correlate the results in cases in which the local lesion has been repaired with those in a group in which no surgical intervention has been carried out.

TABLE 9.—*Cumulative Mortality Figures in an Observed Group of 199 Patients with Spinal Dysraphism**

Age at Time of Death, Mo.	No.	Per Cent
1 or less	15	7.5
3 or less	34	17.0
6 or less	53	26.6
12 or less	67	33.6

* Of the remaining 132 cases not tabulated here, 16 patients died between the ages of 1 and 12 years, 76 are alive, and the details of 40 are unknown.

The localization of the lesion about the infant's head resulted in surgical removal in 80.7% of cases, while only 39.2% of the patients with spinal lesions were operated upon. Of the 26 encephaloceles in this series, 5 had no plastic repair. Because this series is small and because follow-up examinations are lacking in 13 instances, no conclusions are warranted from a comparison of results with and without surgery in the cranial group.

On rare occasions an untreated meningocele or myelomeningocele will survive until adulthood. The usual course is death due to rupture and meningitis or to complications such as hydrocephalus or urinary or pulmonary infection. In the spinal group of 83 who died, meningitis was the most frequent cause (Table 8). In the group of 121 patients who were not operated upon, meningitis was recorded as the cause of death in 28 or 23.14%. In the series of patients for whom operations were done, meningitis was listed as the cause of death in 5 of 78, or 6.41%. The plastic repair which successfully replaces a firm integument for the extremely thin cyst wall will preclude accidental rupture, sepsis, and meningitis.

In the spinal group of 199 patients, 51 were excluded, because of inadequate follow-up data (38 patients), because they were stillborn (4 patients), or because they were operated upon after the age of one year (9 patients). Of the remaining 148 patients, 58 were operated upon during the first year of life. At one year 54

of this group were alive and only four were dead. In the series of 90 patients not operated upon, there were 23 alive, whereas 67 had died by the age of one year.

In applying the statistical chi-square test to these data, one finds a significant increase in the number of patients operated upon who survive. However, this value of chi-square may not be valid, because it must be assumed that the patients whose conditions were more hopeful were operated upon and that patients were not selected for operation in a random manner.

PARENTAL AGE

The relation of parental age to the occurrence of malformations was studied by Murphy [10] from two points of view: the age of the mother at the birth of the child and the difference in ages of the parents. He concluded that malformed children were born to older mothers more often than to young ones. The mothers in his series married at 21.1 years and bore the first normal child at 23; the first defective child was not born until the mother was 28.4 years old. In this series the average age of 195 mothers was 25.8 years. When compared to the average age (25.52 years) of 3,257 mothers who were delivered in the department of obstetrics in the years, 1928, 1938, and 1948, and examined by statistical analysis, there was no significant difference in maternal age of the control group and those with cranial and spinal malformations.

Murphy [10] also observed that parental age difference is not a factor in the production of congenitally malformed children. The average differences in ages of fathers and mothers in the present series of meningoceles, myelomeningoceles, and encephaloceles (sample of 193) is 3.97 years. The average difference in ages of fathers and mothers as taken from the records of 188,023 birth certificates in 1947, 1948, and 1949 in the state of Iowa is 3.39 years. When these figures are subjected to statistical analysis there is no significant difference, at least at the 95% level.

BIRTH RANK AND WEIGHT

Murphy [10] determined that later-born children (after birth rank four) were found to be malformed more often than their earlier-born siblings. The pregnancy number for the 211 cases in which these data were known in this series averages 2.56.

Murphy [10] concluded that malformed offspring were born prematurely more than four times as often as their normally developed siblings. The birth weight was recorded in 182 infants in this series, with an average of 7.37 lb. (3,289 gm.). Of the 203 patients for whom birth data were available, 175 (86.3%) were listed as being full-term and, only 10 (4.9%) were said to be premature. The percentage of premature infants (2,500 gm., or 5 lb., 8 oz., as upper boundary) in the general population is said to be 11.7%.[37] It would seem that the congenital abnormalities under discussion have little effect on the maturity of the infant.

LABOR

Labor was listed as "normal," spontaneous, and vertex in 118 cases (58.2%). Cesarean section was performed in seven cases (3.4%). Two of these were indicated by previous section. Eastman [37] states that the incidence of Cesarean

37. Eastman, N J.: Williams' Obstetrics, Ed. 10, New York, Appleton-Century-Crofts, Inc., 1950.

section in the United States is "about 2%." Forceps were used in 20 cases (9.9%). Breech presentation occurred in 12 cases (5.9%), which is higher than the usual incidence (2.8 to 3.30%).[37] In 22 cases (10.8%) the birth data were incomplete.

Labor was said to have been "difficult" in 24 cases (11.8%). Bourgeois and Spencer [38] reported their experience with dystocia caused by a meningocele. The infant's head was delivered by elective low forceps, and after no further progress the feet were delivered, but the mass remained incarcerated in the uterus until the cyst ruptured. Blochas [39] reported the rupture of a fetal myelocele as a cause of hemorrhage during the second stage of labor. Such experiences are apparently rare. Faber and Ericksen [40] reported the prenatal diagnosis of a spina bifida when roentgenograms were taken to clarify a breech presentation.

TWINS

Fry [41] reported spina bifida in binovular twins, the dizygotic origin being confirmed by two separate placentae and chorions. He cited the only case of spina bifida in uniovular twins as that reported by Eskelund and Bartels.[42] Wright [43] reported upon a pair of twins, each with a syringomyelocele. In the present series one girl infant exhibited lumbosacral lipomeningocele. Her twin sister was described as "perfectly normal." There was one set of twins, conjoined at the midsacral region, with spina bifida and a large, low lumbar myelomeningocele contributed to by each twin. These infants had a single placenta and chorionic membrane. There were multiple associated anomalies. These infants were the products of a full-term gestation, and delivery was spontaneous after a labor of 19 hours. The parents gave a history of twins in both families but knew of no other "Siamese twins." The twins died at the age of 4½ months. Dawson [44] published a report of dissection of the thorax, abdomen, and pelvis.

MONTH OF CONCEPTION

Petersen [45] studied the seasonal trend in conception in malformations. He has compared the regional incidence of malformations to storm and cyclone tracks and to changes in barometric and meteorologic conditions. He reported the highest incidence of spina bifida in the spring months, April, May, June, and part of July. Murphy [10] studied the month of conception for 935 malformed persons and for their normally developed siblings and found a slight preponderance of conception of the malformed in the summer months. The presumed month of conception

38. Bourgeois, G. A., and Spencer, R. F.: Dystocia Caused by Meningocele with Coincidental Dermoid Cyst, New York J. Med. **46**:2534-2535, 1946.

39. Blochas, M.: Rupture of Fetal Myelocele as Cause of Hemorrhage During Second Stage of Labor, Medicina, Kaunas **22**:245-246, 1941.

40. Faber, L. A., and Ericksen, L. G.: Prenatal Diagnosis of Spina Bifida, J. Iowa M. Soc. **26**:359-361, 1936.

41. Fry, A.: Spina Bifida in Binovular Twins, Brit. M. J. **1**:131-132, 1943.

42. Eskelund, V., and Bartels, E. D.: Spina Bifida Umbalis in Uniovular Twins, Nord Med. **11**:2075-2079, 1941.

43. Wright, H. A.: Twins, Each with Syringomyelocele, Canad. Proc. & Rev. **25**:205, 1899.

44. Dawson, H.: Pyopagus Twins, Report of Dissection of the Thorax, Abdomen and Pelvis, Am. J. Dis. Child. **68**:395-404, 1944.

45. Petersen, W. F.: Seasonal Trend in the Conceptions of Malformation, Am. J. Obst. & Gynec. **28**:443, 1934.

could be calculated in 210 cases of the present series. Table 10 reveals a preponderance of conceptions leading to these malformations in the spring. The statistical chi-square test was done on the above data and disclosed that there is no significant variation in the conception rate from month to month.

REPETITION OF MALFORMATIONS AMONG SIBLINGS

From the dearth of published instances in the literature one might be led to believe that spinal dysraphism occurs in siblings with great infrequency. Shulman [46] reported its occurrence in two successive children of the same family. Woltman [47] found that in 2 of 187 cases there was presumptive evidence of spina bifida in other members of the family. In 3 of Cutler's [35] series of 62 cases there was a history of spina bifida or hydrocephalus in other siblings. Sachs [48] referred to a family in which three successive children had spina bifida. Murphy,[49] in a study of duplication of malformations among siblings, reported four families with two or more cases of spina bifida. Early reports of presence of spina bifida in more than

TABLE 10.—*Month of Conception*

Month	No.	Per Cent
Jan.	21	10.0
Feb.	14	6.7
March	21	10.0
April	23	10.7
May	24	11.4
June	10	4.8
July	18	8.6
Aug.	19	9.1
Sept.	15	7.0
Oct.	19	9.1
Nov.	10	4.8
Dec.	16	7.6
Total	210	100.0

one member of a family were made by Butler-Smythe,[50] Wright,[13] and Pendelton.[51] Pybus [52] described a family in which four children had congenital defects of the spine. In Ingraham and Swan's [7] series, spina bifida in the family was admitted to in 16 of 277 cases (6%). Approximately an equal number had other anomalies. Wilner [53] reported a myelomeningocele in an infant born to a mother who had a

46. Shulman, B. H.: Spina Bifida with Meningocele: Occurrence in 2 Children of Same Family, Arch. Neurol. & Psychiat. **47**:474-476, 1942.

47. Woltman, H. W.: Spina Bifida: Review of 187 Cases, Minnesota Med. **4**:244, 1921.

48. Sachs, E., in Abt, I. A.: Pediatrics, Vol. 7, Philadelphia, W. B. Saunders Company, 1925, Chap. 159, p. 93.

49. Murphy, D. P.: The Duplication of Congenital Malformations in Brothers and Sisters and Among Relatives: A Study of Sibling Defects in 40 Consecutive Families, Surg. Gynec. & Obst. **63**:443, 1936.

50. Butler-Smythe, A. C.: Spina Bifida and Hydrocephalus Occurring in the Same Family, Lancet **1**:272, 1889.

51. Pendelton, E. M.: Spina Bifida: Three Cases from One Mother, South. Med. & Surg. **13**:215, 1857.

52. Pybus, F. C.: Spina Bifida, Lancet **2**:599, 1921.

53. Wilner, I. A.: Familial Repetition of Myelomeningocele, J. Michigan M. Soc. **48**:727-729, 1949.

similar defect at birth. Hamby [24] described the case of a 20-year-old woman with spina bifida occulta and bifid spinal cord separated by a bridging bony process (diastematomyelia). Her older sister had spina bifida, and the patient's grandmother had a similar condition. The patient's baby had a spina bifida with a bifid spinal cord and died at 3 weeks of meningitis.

In this group of 224 families, anomalies were denied in 123 cases (55%). In 40 other families (18%) this information was not known. Sixty-one (27%) admitted to a total of 106 anomalies. These are listed in Table 11.

Meningoceles, myelomeningoceles, or encephaloceles were acknowledged in 11 siblings representing seven families. In 126 families in which repeated births occurred, spina bifida or cranium bifidum occurred twice or more in 7 families. If one assumes the incidence to be 1 in 1,000 in the usual population, it appears that the incidence of this deformity among families in which the deformity has already occurred once is 56 times the incidence in the general population, or 1 in 18.

TABLE 11.—*Abnormalities Admitted to in Sixty-One Families (27.2%)*

Abnormality	No.
Spinal or cranial dysraphism in siblings	11
Other deformities in siblings	26
Spina bifida in relatives	20
Spinal "deformities" in relatives	5
Deformed children in relatives	8
Hydrocephalus	4
Cleft lip, palate	7
Club feet, dislocated hips	8
Mental deficiency	8
Deaf-mutism	3
Convulsive disorder	2
Pilonidal	2
Imperforate anus	1
Web digits	1
Total	106

In 126 families with repeated births, spinal or cranial dysraphism and some other anomaly occurred in 22 families. The usual frequency of malformations in the general population is 4.7 in 1,000, or 1 in every 213.[10] If we assume this to be approximately true, it appears that the incidence of any deformity among families in which meningocele, myelomeningocele, or encephalocele has occurred is 37 times the incidence of any deformity in a normal population. This incidence is 174 in 1,000, or 1 in 6. Murphy [10] reported that in families already possessing a malformed child, one infant out of every eight subsequent births was malformed, the defect in the first was duplicated in a subsequent malformed member in nearly one-half of the instances.

The highly significant increase in incidence of cranial and spinal dysraphism in females constitutes presumptive evidence in favor of heredity as a causative factor of these lesions. The frequent duplication of defects in siblings and the high incidence of malformations in relatives support this view. If spontaneously occurring malformations arose primarily from environmental influences, it would seem that all types of congenital defects would affect both sexes with equal frequency. It is therefore suggested that the malformations under discussion arise from factors inherent in the germ cells prior to fertilization.

SUMMARY AND CONCLUSIONS

The subject of spinal and cranial dysraphism is reviewed. The details of a survey of 225 meningoceles, myelomeningoceles, and encephaloceles are presented and discussed.

The following conclusions are selected for emphasis:

The incidence of meningoceles, myelomeningoceles, and encephaloceles is about 1 in 1,000 births. Females outnumber males in the ratio of 1.6 to 1. In three-fourths of the 199 patients with spinal dysraphism the lesion was classified as a myelomeningocele.

Ninety-nine (44%) of the 225 patients were subjected to operation. The operative mortality was 8.0%.

At the present time 20% of the patients with meningocele or myelomeningocele and 30% of those with encephaloceles are classified by the parents as "well" and unhampered by any significant incapacity from their anomaly.

One hundred cases presented 217 associated congenital anomalies (excluding club foot, dislocated hip, and hydrocephalus).

The incidence of these cranial and spinal malformations among families in which the deformity has already occurred once was 56 times (1 in 18) the incidence in the population at large (1 in 1,000).

The incidence of any deformity among families in which meningocele, myelomeningocele, or encephalocele has occurred was 37 times (1 in 6) the incidence of any deformity in the general population (1 in 213).

The preponderance of cranial and spinal dysraphism in females and the incidence of abnormalities in the relatives constitute presumptive evidence in favor of a familial factor in the cause of these lesions.

INTRAVENOUS IRON THERAPY IN IRON-DEFICIENCY ANEMIA OF INFANCY AND CHILDHOOD

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IRON-DEFICIENCY anemia is more obviously of nutritional origin in infancy than in later years when complications of bleeding, infection, or depressive chronic disease are more likely to enter into the pathogenesis. Also, iron-deficiency anemia occurs much more commonly in infancy and early childhood than is generally recognized. The rapid growth of the cellular tissues and the blood volume and the concomitant increase in the absolute mass of circulating hemoglobin tend to deplete the iron reserves unless a liberal intake of nutritional iron passes the intestinal barrier and is absorbed into the body. This is the basis for the aphorism that the infant bleeds into his own increasing blood volume.[1] Since a milk diet is almost devoid of iron, the infant must have a liberal intake from other sources, or else he must draw on storage iron for blood formation and thereby exhaust his reserve supply.

About one-fourth of the total body iron is in myohemoglobin and the parenchymal enzymes, cytochrome, catalase, and peroxidase. Since these are husbanded regardless of stresses imposed by disease, they jointly compose what is known as the immobile iron fraction.[2] The remaining three-fourths of the body iron, present in hemoglobin and stored in the liver, spleen, and bone marrow, is mobilizable for and utilized in hemopoiesis. Ferritin, hemosiderin, and inorganic ferrous iron appear to be as readily available for hemoglobin formation as the iron liberated by the destruction of effete red cells.

When the internal iron supplies are inadequate, the erythrocytes contain less than their normal complement of hemoglobin and tend to be small and hypochromic. In more severe and prolonged cases the red blood cell count falls also. The hemoglobin content of unit volumes of blood is also diminished. The erythroid marrow responds to the deficiency state by assuming a hyperplastic appearance, usually with

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1. Heath, C W., and Patek, A. J.: The Anemia of Iron Deficiency, Medicine **16**:267, 1937.
2. Hahn, P. F.: Metabolism of Iron, Federation Proc. **7**:493-498, 1948.

hemoglobin-deficient erythroblasts. When iron is then supplied, the active synthesis of hemoglobin is quickly reassumed and the red cells mature once more in normal fashion, giving rise to a phase of transient reticulocytosis.

Studies with the radioactive isotopes of iron during the last decade have contributed greatly to knowledge of the metabolism of iron. With the Fe^{59} isotope it has been possible to recognize the presence of recently administered iron in plasma and soon afterwards in the red cell hemoglobin, and to show that in iron-deficiency anemia the absorption rate can be increased many times over normal. That the anemia per se does not influence the intake of iron is seen from the fact that normal dogs, bled acutely of 60% of their estimated blood volume, when fed tagged iron absorbed no more than when in the normal state. However, if a week or so is allowed to elapse following the hemorrhage, the intake of tagged iron becomes several times greater than normal.[2] Such observations have led to the conception of an acceptor mechanism in the gastrointestinal mucosa which bars the transit of iron through the intestinal mucosa when the body is well saturated with iron but permits its passage when iron is needed. The ferritin, principally of the duodenum, is considered to be in equilibrium with the plasma iron. As the plasma iron is lowered, the mucosal ferritin gives up iron to the plasma, and iron from the intestinal tract enters the mucosa. The absorbed iron, again oxidized to the ferric form, combines with plasma globulin (beta globulin, or fraction IV)[3] for distribution to the other tissues. The efficiency of this absorptive process parallels the need for the element.[3] The iron-protein complex, ferritin, is believed to be the factor regulating the absorption of iron by the intestinal mucosa.[4]

Iron administered orally in humans appears to be absorbable only when in the reduced or ferrous form. Ferric ions (Fe^{+++}) taken by mouth are reduced by the hydrochloric acid of the stomach to the ferrous (Fe^{++}) state. When hypochlorhydria or achlorhydria is present, as occurs in all forms of nutritional anemia, the process is retarded or inhibited. The reduction of ingested ferric iron is then delayed, and the deficiency state becomes aggravated.

Iron deficiency can almost always be treated effectively by oral administration of appropriate amounts of iron salts, preferably ferrous salts, though complete absorption is never reached even when the amount administered is as small as 1 mg. No one would question the value of proper oral iron therapy, but its occasional shortcomings are undeniable. It can be seen from Table 1 that the utilization of all oral forms of iron is considerably less than the utilization of iron administered intravenously. The percentage of utilization of orally administered iron, small as it is, holds true only when the intestinal absorption mechanisms are operating efficiently.

In 1947 Nissim[5] revived interest in the giving of iron intravenously by showing that a solution of iron oxide in combination with soluble high-molecular carbohydrates could be prepared which caused no serious reaction when given intravenously in quantities containing as much as 1,000 mg. of elemental iron. Such saccharated

3. Darby, W. J.: Iron and Copper, J. A. M. A. **142**:1288-1295, 1950.

4. Laufberger, M.: Sur la cristallisation de la ferritin, Bull. Soc. chim. biol. **19**:1575, 1938. Granick, S.: Ferritin: IV. Occurrence and Immunological Properties of Ferritin, J. Biol. Chem. **149**:157, 1943; Ferritin: IX. Increase of Protein Apoferritin in Gastrointestinal Mucosa as Direct Response to Iron Feeding: Function of Ferritin in the Regulation of Iron Absorption, ibid. **164**:737, 1946.

5. Nissim, J. A.: Intravenous Administration of Iron, Lancet **1**:49-51, 1947.

preparations of iron oxide do not flocculate when they come in contact with blood plasma, and so emboli are not formed. It is this compatibility with serum that gives them a low toxicity.

In the past few years a number of clinical reports have appeared describing satisfactory rises in hemoglobin levels in adult patients with iron-deficiency anemia [6] in response to intravenous injections of saccharated iron preparations. These have shown a utilization approaching 100%.[7] This present report describes clinical experiences with such a preparation in the treatment of iron deficiency anemia in infancy and early childhood. Special attention was given to the clinical and hematologic responses and the circumstances attending the development of toxic reactions.

METHOD OF STUDY

This study is based on the responses of 80 infants and children with anemia to intravenous injections of saccharated iron oxide. The solution of saccharated iron oxide used in this study

TABLE 1.—*Utilization of Iron**

Preparation	Daily Dose, Gm. or Cc.	Iron Content, Mg.	Utilization, %
Metallic			
Reduced iron	1.5-6.0	1,200-5,000	0.5-2.0
Ferrous chloride	0.25-0.5	100-200	12.5-25.0
Ferrous sulfate, exsiccated	0.6	180	14
Ferrous carbonate (Blaud's pill)	3.0-4.0	300-400	6-8
Ferrous			
Ferrous lactate	1.5	300	8
Iron perchloride solution	8.0	400	6
Ferric citrate	2.0	400	6
Ferric hydroxide	30-45	1,500-2,250	1.1-1.7
Ferric			
Soluble ferric oxide	35	1,000	2.5
Complex Ferric			
Ferric ammonium citrate	4.0-8.0	800-1,600	1.5-3.0
Saccharated iron oxide (intravenous)	5.0-10.0	100-200	100
Injection			
Injection of iron, B. P. (intramuscular)	5.0-10.0	16-32	100

* Compiled from sources in the medical literature.

was "feojectin" (Smith, Kline & French Laboratories). The criterion for anemia was a hemoglobin level of 9 gm. or less per 100 ml. of serum. The subjects were taken, without selection,

6. Davidson, L. S., and Girdwood, R. H.: Refractory Iron Deficiency Anemia Treated with Intravenous Saccharated Oxide of Iron, Brit. M. J. **1**:733, 1948. Slack, H. C. B., and Wilkinson, S. F.: Intravenous Treatment of Anemia with an Iron-Sucrose Preparation, Lancet **1**:11-14, 1949. Govan, A. D. T., and Scott, S. M.: Intravenous Iron in the Treatment of Anemia of Pregnancy, ibid. **1**:14-16, 1949. French, D. C.: Intravenous Treatment of Anemia with an Iron Sucrose Preparation (Letters to Editor), ibid. **1**:370, 1949. Holly, R. C.: Iron Metabolism in Pregnancy, Bull. U. Minn. Hosp. **20**:475, 1949. Andersson, N. S. E.: Experimental and Clinical Investigation into the Effect of Parenterally Administered Iron, Acta med. scandinav., Supp. 241, p. 5-71, 1950. Horrigan, D. L.; Mueller, J. F., and Vilter, R. W.: Observations on the Intravenous Administration of Saccharated Oxide of Iron in Human Beings, J. Lab. & Clin. Med. **36**:422, 1950. Brown, E. B.; Moore, C. V.; Reynatarje, C., and Smith, D. E.: Intravenously Administered Saccharated Iron Oxide in the Treatment of Hypochromic Anemia: Therapeutic Results, Potential Dangers and Indications, J. A. M. A. **144**:1084-1089, 1950.

7. Mugrage, E. R., and Andresen, M. I.: Values for Red Blood Cells of Average Infants and Children, Am. J. Dis. Child. **51**:775-791, 1936.

as diagnosed in the outpatient department or in the wards of the Children's Hospital, Philadelphia, and were divided into two groups.

Group 1 (66 patients) comprised all those with iron deficiency brought about by a deficient dietary intake of iron, often complicated by a history of prematurity, multiple births, or previous infection. The maternal intakes of iron during pregnancy were not known. The results of blood examinations were used in making the diagnoses. Nearly all these patients were followed and treated as outpatients, without hospitalization. More adequate diets were not advised until the second or third week of observation, as a rule, but the improved appetite after the first few days was promptly followed in many instances by a greater food intake, inevitably including some iron-containing vegetables and meats. Ten of these infants had shown no satisfactory improvement of their anemia after previous adequate oral iron therapy.

Group 2 (14 patients) comprised all others, in whom the anemia was associated with miscellaneous infections or toxic disturbances, such as tuberculosis, rheumatic fever, nephritis, or lead poisoning. Nearly all in this group were in the hospital wards and receiving a balanced diet with ample protein content.

The dosage of saccharated iron oxide was calculated on the need for enough iron to correct the deficiency in both the circulating hemoglobin and in the tissue depots. The amount of iron thought necessary to restore the circulating hemoglobin to normal was determined by first calculating the total hemoglobin iron in a normal subject of the same weight. A value of 44 ml. of whole blood per pound (0.5 kg.) of body weight was taken as the approximate normal blood volume of the child, and a hemoglobin level of 12.5 gm. per 100 ml. was taken as the desired level to be attained. There is approximately 0.003 gm. of iron in every gram of hemoglobin. The following equation was then used to calculate the deficit:

$$\text{Mg. Iron Deficit} = \frac{\text{B.W.} \times 44 \times 12.5 \times 0.003 \times 1000}{100} - \frac{\text{B.W.} \times 44 \times \text{Hg.} \times 0.003 \times 1000}{100}$$

B. W. = body weight in pounds.

Hg. = patient's hemoglobin in grams per 100 ml.

This formula can be algebraically simplified to read

Mg. Iron Deficit = body weight in pounds $\times$ (16.5 — 1.3 $\times$ present hemoglobin level in grams per 100 ml.)

The dose thus calculated was then arbitrarily doubled, in order to correct for the depleted body stores of iron.

The amount of iron given was divided into doses consisting of 50 to 100 mg. the first day and 100 mg. daily thereafter until the total was reached. Since giving the original series of injections, we have observed four moderately severe reactions in infants under one year old. It now seems advisable in this age group to start with an initial dose of 25 mg. and use 50 mg. daily thereafter until the calculated dosage has been given.

Each 5-ml. ampule of the preparation contains 100 mg. of iron. This is administered intravenously. The needle is inserted into the lumen of the vein with care, since extravasation is difficult to detect because of the dark-chocolate color of the preparation. As a precaution before commencing injection, 2 to 4 ml. of blood is first withdrawn into the syringe and mixed with the iron suspension. No other diluent is employed. Experience elsewhere has shown that injections given rapidly are frequently followed by reactions. Hence five to eight minutes should be taken for injection of the iron suspension.

The hematologic studies were made on capillary blood flowing freely from the fingertip. Erythrocyte counts were made with hemocytometer chambers and pipettes certified by the United States Bureau of Standards. Hemoglobin levels were measured photoelectrically, using an Evelyn photoelectric colorimeter and reference curves calibrated against Drabkin's copper ammonium sulfate standard. Hematocrit readings were determined by the Van Allen method using standard Van Allen tubes; the anticoagulant was a 1.6% solution of sodium oxalate in distilled water, and the centrifuging was done at 3,000 rpm in an International centrifuge No. 1. Reticulocytes were enumerated in smears stained vitally with brilliant cresyl blue.

On the day of the patient's first visit, in addition to the history and physical examination, the red blood cell count, hemoglobin level, and white cell and differential counts were determined,

as well as the reticulocyte count, hematocrit determination, estimation of the Wintrobe constants, sickling test of Negroes, and bone-marrow aspiration when feasible.

Studies were repeated on the 1st, 2d, 4th, 6th, 9th, and 13th days, with the exception of the bone-marrow aspirations, sickling tests, and leucocyte counts. The patients were then seen weekly for the next 11 weeks and monthly thereafter.

The children with iron-deficiency anemia ranged in age from 2 months to 6 years. The great majority (91%) were between 6 and 30 months old (Table 2). The mean arithmetical age was 15½ months. A total of 159 injections were given. Each child received one to six injections, the average number being two and two-fifths. The average total dose of saccharated iron oxide was 239 mg.

RESULTS

Hemoglobin Levels.—The initial hemoglobin levels before therapy ranged from 2.5 to 9 gm., with a mean of 7.5 gm. The daily rise in hemoglobin level was recip-

TABLE 2.—*Distribution by Age of Sixty-Six Patients with Hypochromic Anemia*

Age, Mo.	Males	Females	Total No.	Total %	
0-6	0	2	2	3.03	
6-12	9	7	16	24.2	91%
12-18	19	6	25	38	
18-24	9	3	12	18.2	
24-30	7	0	7	10.6	
30-36	0	1	1	1.5	
36	2	1	3	4.5	

TABLE 3.—*Relationship of Reticulocyte Response and Daily Rise in Hemoglobin Level to Initial Hemoglobin Level for Sixty-Six Patients*

Patients, No.	Range of Initial Hb. Level, Gm.	Average Peak of Reticulocyte Response, %	Average Daily Rise in Hb. Level, Gm.	Post-Treatment Day Reticulocyte Peak, Average	Initial Red Cell Count, Millions/Cu. Mm.	Initial Hematocrit Value, %
5	5	14.6	0.28	4.2	2.2	11.7
9	5-5.9	12.6	0.20	4.8	3.5	19.5
7	6-6.9	4.5	0.21	6.4	4.2	24.2
12	7-7.9	4.38	0.13	4.6	4.6	25.1
33	8-9	3.4	0.14	6.0	4.4	27.5

rocally proportional to the initial reading, as shown in Table 3. The average daily rise in hemoglobin level was 0.155 gm.; it was detectable as early as the second day and reached a mean high level of 12.5 gm. per 100 ml. at about the 32d day. This maximum corresponds exactly with the amount sought by the calculated formula. After the 32d day the mean fluctuated between 10.5 and 12.5 gm. for the group of infants who were followed for as long as 70 days thereafter. With one exception, every child with iron-deficiency anemia had a rise in hemoglobin level (Fig. 1) to above 10 gm. per 100 ml.

Erythrocyte Counts.—Changes in the erythrocyte counts were not as striking as in the hemoglobin levels. The initial readings ranged from 1,810,000 to 5,360,000. The means of all initial readings rose from 4,200,000 before therapy to 4,500,000 after therapy.

Only with mean initial hemoglobin levels below 7.0 gm. was erythrocytopenia observed; with levels of 7.5 gm. and upward the red blood cell counts were in the

post-treatment range (Table 3). When anemia was severe enough to depress the red cell count, the mean rates of rise in both the hemoglobin level and the red cell count were equal until a mean red cell count of 3,500,000 was reached; above this the restoration of the red cells outstripped that of the hemoglobin. All these observations demonstrate that hemoglobinopenia, microcytosis, and a diminished hematocrit value are much more sensitive indicators of iron-deficiency anemia in early childhood than is erythrocytopenia.

Reticulocytes.—Prior to therapy, 26 of the 66 patients had a reticulocytosis greater than 2.0%, and 7 had readings somewhat higher than 4.0%. Every child exhibited a marked rise in reticulocyte percentage after receiving iron intravenously. This rise typically became apparent on the second or third day, reached its peak between the fifth and sixth day, and subsided within a few more days. The extent of the rise was inversely proportional to the initial hemoglobin level (Table 3). The

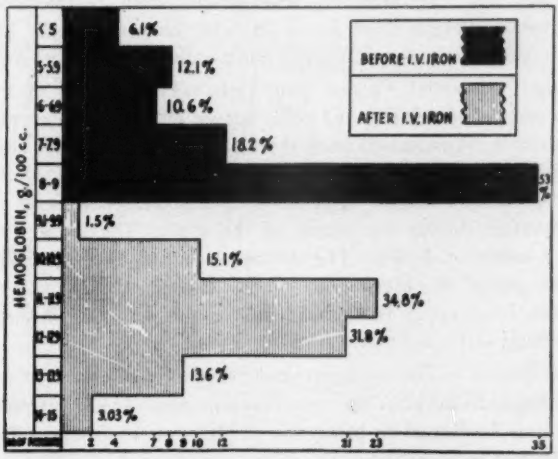

Fig. 1.—Distribution by hemoglobin levels of 66 children with hypochromic anemia, before and after therapy with saccharated oxide of iron.

highest rise noted in the sequence of determinations was a reading of 31.2% in an infant with an initial hemoglobin level of 5.4 gm. In many of the children a mild reticulocytosis continued for several weeks after the injections were stopped.

Hematocrit.—The mean initial volume of packed red blood cells was 25.6%. Four specimens were less than 20%, and all but two were 30% or lower. The mean curve showed a rapid rise after treatment was begun. On the 6th day the mean was 29.1%; on the 19th day, 33.1%; on the 32d day, 33.4%. The curve then oscillated between 33.2 and 37.5% until the 100th day and later. The mean hematocrit values reflected the corresponding hemoglobin levels with approximate faithfulness and were not correlated with the red cell counts. The hematocrit readings in individual patients displayed wider fluctuation in day-to-day readings than did the erythrocyte counts, whereas the hemoglobin determinations seemed the least variable. Occasional high hematocrit readings seemed more likely to be due to technical than to physiologic causes. The calculated indices of mean corpuscular

hemoglobin which excludes the hematocrit value exhibited less variation than did the mean corpuscular volume and hemoglobin content of packed red cells, each of which includes this parameter.

Mean Cellular Hemoglobin.—The average quantity of hemoglobin in the individual red cell is calculated from the figures for hemoglobin level and erythrocyte count. The mean initial value before treatment was 19.3 micromicrograms; in four specimens the value was 12 micromicrograms, and in all but one it was below 29 micromicrograms. The mean curve rose slowly, to reach an inconstant plateau between 26.0 and 28.0 γ on the 25th day. This corresponds to the normal zone found by Mugrage and Andresen [7] in infants between 4 and 18 months old, and by Guest, Brown, and Wing [8] for infants and children from 7 months to 4½ years old.

Mean Cellular Volume.—The size or volume of the average single erythrocyte corpuscle is estimated from the hematocrit reading and erythrocyte count. The mean initial reading before therapy was 60.8 cubic microns. The lowest individual value was 40 cubic microns. The mean size rose steadily after treatment was begun, to reach an inconstant plateau from 74 to 78 cubic microns by the 17th day. This corresponds to Guest, Brown, and Wing's mean value of 74 for children 2 years old.

Hemoglobin Content of Packed Red Cells.—The content of hemoglobin as related to the mass of circulating red cells, known also as mean corpuscular hemoglobin concentration, is estimated from the blood hemoglobin level and the hematocrit value. The percentage reading is the numerical equivalent of the number of grams of hemoglobin per 100 ml. of packed red cells. This parameter exhibited little significant alteration during the course of the study. The initial readings before therapy had a mean of 31.4%. The means oscillated between 28.6 and 34.9% throughout the period of observation. Guest, Brown, and Wing.[8] had noted for normal children from upper economic levels in this age period that most of the individual readings fell consistently between 34 and 35%.

Clinical Responses.—The comment most frequently offered by the mothers was that the child began to eat after the very first injection. This is probably the reason why most parents continued to bring the children in for frequent follow-up tests. Along with the rise in hemoglobin the pallor disappeared, and the vigor and sense of well-being returned.

The following reports illustrate the favorable clinical and hematologic responses that were customarily attained in the more severe cases.

CASE 1 (Fig. 2).—G. M., a Negro girl, was brought to the clinic shortly after her first birthday because of vomiting and fever of 24 hours' duration. Upon physical examination the patient was found to be very pale; she appeared acutely ill and slightly dyspneic. The chest was clear. The heart showed no murmur. The pulse rate was 200 per minute. The liver and spleen were not palpable. The blood count on admission revealed a hemoglobin value of 2.5 gm., 1,900,000 red blood cells, reticulocyte count of 1.4%, hematocrit reading of 10%, and 25% hemoglobin in the packed red cells. The bone marrow showed marked erythrocytic hyperplasia. The child's diet had always consisted of 2 qt. (1.8 liters) of milk daily; solid food had never been taken. One month previously she had reduced her intake to about 1 qt. (0.9 liter) a day. Four successive daily doses of 100 mg. of saccharated iron oxide were administered intravenously. There were no reactions. In two weeks the hemoglobin level had risen to 10 gm. and the red

8. Guest, G. M.; Brown, E. W., and Wing, M.: Erythrocytes and Hemoglobin of the Blood in Infancy and in Childhood: II. Variability in Number, Size, and Hemoglobin Content of the Erythrocytes During the First 5 Years of Life, Am. J. Dis. Child. **28**:458-463, 1934.

cell count to 3,520,000. At four weeks the hemoglobin level was 12.7 gm. and the red cell count 4,610,000. Appetite improved almost at once. Reticulocytes rose to 17%. The mean cell volume rose from 52.1 to 92 cubic microns in four weeks, and the hemoglobin content of the packed red cells from 25 to 36 micromicrograms. At this time the child appeared healthy, active, and alert.

CASE 2.—R. O., a 22-month-old Negro boy, was admitted to the Children's Hospital, Philadelphia, on Aug. 7, 1950, because of constipation and vomiting. Since the age of one week he had had bowel movements only after a laxative or enema. With severe constipation, vomiting occurred. The child had never walked or sat up. The birth history was normal. Upon physical examination the tonsils were found to be hypertrophied. The liver was felt 1 cm. below the costal margin, and the spleen was not palpable. Rectal examination revealed moderate fecal impaction. The impression upon admission was congenital megacolon. The hemoglobin level was 9 gm. per 100 ml.; the red blood cell count, 5,200,000; the hematocrit reading, 29%; reticulocytes, 0.6%; mean cellular hemoglobin, 17.3 micromicrograms; mean cellular volume,

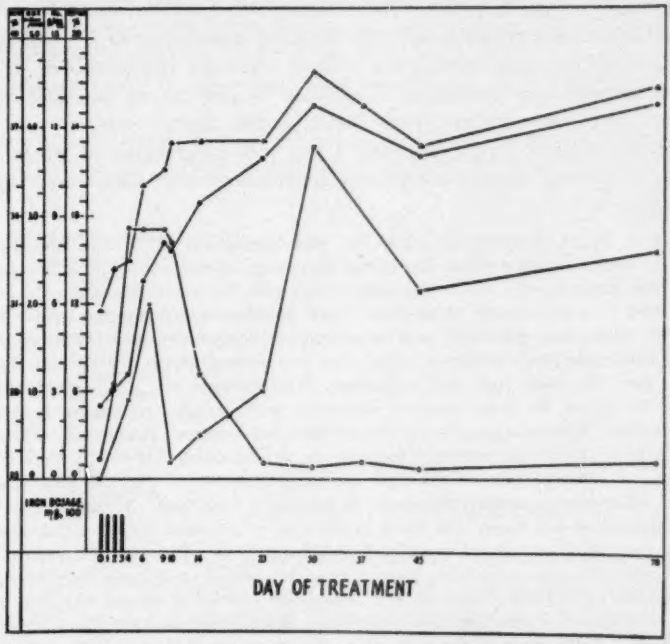

Fig 2.—Responses of G. M. (Case 1) to intravenous injections of saccharated iron oxide. Note the almost immediate reticulocytosis and the prompt rise in red cell count and hemoglobin levels. Solid dots indicate hemoglobin; triangles indicate red blood cells; circles indicate reticulocytes, and crosses indicate mean cell hemoglobin concentration. The fluctuations in the mean cell hemoglobin concentration are presumably due to technical error.

55.7 cubic microns, and hemoglobin content of packed red cells, 31%. The leukocyte count was normal. The red cells appeared hypochromic in the direct smear, with moderate anisocytosis and poikilocytosis. No sickling was found upon testing. Saccharated iron oxide, 100 mg., was injected on Aug. 10, 1950, and 50 mg. on the next day, with no untoward reaction. The reticulocyte count increased to 2.4% six days after the first injection. By Aug. 17 the appetite had markedly increased. A final blood count on Sept. 30 revealed a hemoglobin level of 13.5 gm., red blood cell count of 4,970,000, hematocrit reading of 36%, reticulocyte value of 0.4%, mean cellular hemoglobin value of 27.1 micromicrograms, mean cellular volume of 72.4 cubic microns, and hemoglobin content of packed red cells, 37.5%. The child had gained 5 lb. (2,300 gm.) in one month and could sit up alone, and the intestinal distention was gone.

Other Forms of Anemia.—The "miscellaneous" group comprised two children with lead poisoning, one with acute glomerulonephritis, one with Still's disease, four with assorted forms of tuberculosis, two with rheumatic fever, one with femoral fracture, one with naphthalene poisoning, one with tetralogy of Fallot, and one with hematuria of unknown cause. Of these 14 patients, satisfactory rises in hemoglobin level (to above 10 gm. per 100 ml.) were obtained in all except a 4-year-old boy with a bone fracture and an 18-month-old girl with rheumatic fever. Excepting these two, the mean hemoglobin level rose from 8 to 11.7 gm. per 100 ml., with a mean daily rise in hemoglobin level of 0.126 gm. This was attained with an average of two and one-half injections representing 259 mg. of iron. Several of these patients had previously received iron orally with no ensuing rise in blood hemoglobin.

Interestingly, of the 12 patients whose hemoglobin levels rose after iron therapy, only 6 exhibited an increase in erythrocyte count amounting to 500,000 cells per cubic millimeter or more, Although a mild to moderate reticulocytosis (2.0% or over) had already been present in 13 of these 14 patients, an additional increase was always noted after therapy. None had an initial macrocytosis.

The following case report describes a boy with tuberculosis in whom a coincident anemia showed marked and prompt improvement after intravenous injections of iron.

CASE 3.—J. W., a 14-month-old white boy, was hospitalized on Dec. 7, 1950, because of fever of one week's duration which had proved refractory to aureomycin, penicillin, and terramycin. When a few months old he had had contact with his maternal grandmother who was later admitted to a tuberculosis sanatorium. Upon physical examination the patient was seen to be a fat, flabby boy, pale, with poor appetite. The temperature was 100 F. rectally; the inguinal lymph nodes were enlarged. The chest was normal except for musical rhonchi on expiration over the whole right side posteriorly. The abdomen was soft, with the liver edge palpable 2 cm. below the costal margin. Urinalysis and tests of cerebrospinal fluid disclosed no abnormalities. The serologic reaction for syphilis was negative; the reaction to a test with old tuberculin (1:1000) was markedly positive; the sedimentation rate was 27 mm. at the end of one hour. A roentgenogram of the chest showed enlargement of the right hilar shadow and a minimal infiltration extending downward in the lower lung field. A diagnosis of primary tuberculous infection was made. The blood at the time of admission showed a hemoglobin level of 7.5 gm. per 100 ml., a red cell count of 3,530,000, per cubic millimeter, a hematocrit reading of 23%, a reticulocyte count of 6.4%, mean cellular hemoglobin of 21.2 micromicrograms, mean cellular volume of 65.1 cubic microns, and hemoglobin content of packed red cells of 32.6%. Doses of 100 mg. of saccharated iron oxide were administered on Dec. 10, 11, and 12. No reactions followed any of these injections. The reticulocyte count rose to 10.5% on the third day after the initial injection. A final blood count on Jan. 1, 1951, showed a hemoglobin level of 13.5 gm., red cell count of 4,470,000, hematocrit of 37%, mean cellular hemoglobin of 30.2 micromicrograms, mean cellular volume of 82.9 cubic microns, and hemoglobin content of packed red cells, 36.5%. The mother's only complaint at the time of follow-up examination was that the child wanted to eat at all times.

COMMENT

Toxicity.—Of 198 intravenous injections only 21 were followed by reactions. Of these, 18 were mild and 3 were moderate; none was severe. Of the mild reactions, one was evidenced by nausea, one by drowsiness, and two by vomiting. One child had a transient swelling of the hand not associated with extravasation, on the side in which the injection had been given in the antecubital fossa. Three children had a generalized papular rash lasting about a day. Ten had mild febrile reactions which might have been missed had the parents not been instructed to take frequent

temperature readings. All of these febrile reactions were associated with one batch of injectable iron and occurred within a few days of each other. When a fresh batch was substituted this manifestation ceased. It was not possible to gather data on subjective symptoms because of the extreme youth of the majority of the patients.

The three moderately severe reactions consisted of fever, with rectal temperature rising to 103 F., which occurred about two hours after injection. The temperature remained high for two to three hours and then dropped abruptly to normal. Every reaction occurred with the first injection. In no case was the reaction severe enough to cause cessation of treatment or to prevent the mother from voluntarily bringing the child in the following day for the next treatment.

Comparison with Blood Transfusions.—The comparative responses of the blood to injections of intravenous iron and to blood transfusion are illustrated in Figure 3. Two infants chanced to be hospitalized on the same day for iron deficiency anemia. Each had blood hemoglobin levels of less than 3 gm. per 100 ml. The first, aged 10 months, was given two transfusions on successive days, one of 200 ml. and one

TABLE 4.—*Untoward Reactions to Intravenous Injection of Saccharated Oxide of Iron*

	Total	Patients with Hypochromic Anemia	Patients with Miscellaneous Anemia
Injections, number	198	159	39
Reactions			
Number	21	21	0
Per cent	10.6		
Mild reactions			
Nausea	1		
Vomiting	2		
Papular rash	3		
Drowsiness	1		
Swelling of hands	1		
Fever	10		
Moderate reactions			
Fever	3		
Severe reactions	0		

of 100 ml. The second infant, aged 11 months, was given 100 mg. of saccharated iron oxide daily for three days. Although the rise of the hemoglobin level and of the red blood cell count was more prompt in the transfused infant, the ultimate response in the one treated with iron was equally satisfactory and more sustained (Fig. 3).

Clinical Applications.—The effectiveness of saccharated iron oxide when iron deficiency exists in childhood can scarcely be questioned. The anemia in nearly all patients who served as subjects in this study would doubtless have improved with adequate oral doses of iron if taken regularly. Several, however, had rejected or vomited or for other reasons had been unable to tolerate oral administration of iron preparations. A few had taken apparently adequate amounts by mouth but had had no evidences of a rise in hemoglobin level.

It is of interest that almost one-fourth of the cases were referred from the surgical clinic. These were children from low-income families who were found to be anemic on physical examination prior to elective surgery. In past years operations for such patients often had to be postponed for several weeks or months while the blood level was being built up by oral administration of iron, or while the child

was hospitalized for one or more transfusions. A few injections of saccharated iron oxide made it feasible to perform necessary surgery within one or two weeks.

In selected situations intravenous injections of iron can serve as an alternative to blood transfusions. Even with the recent great advances in matching and injecting blood, transfusions are not absolutely devoid of danger. Saccharated iron oxide produces no greater incidence of reactions if given slowly and will completely correct an iron-deficiency anemia if it is possible to wait a few weeks for full response. It has the advantage of being much simpler to administer than blood transfusions. There is no need to find and examine donors, cross-match blood, use elaborate equipment, or observe the patient for several hours thereafter.

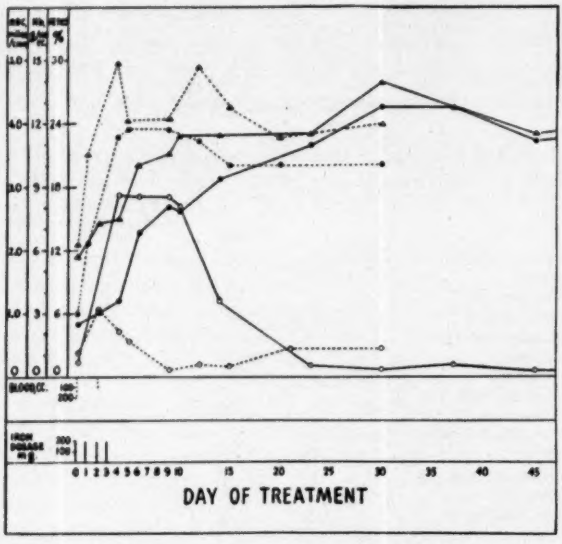

Fig. 3.—Comparison of the blood responses of two infants of equal age to (*a*) saccharated iron oxide (solid line) and (*b*) blood transfusions (broken line). Solid dots indicate hemoglobin level, grams per 100 cc.; triangles indicate red blood cells, millions per cubic millimeter; circles indicate reticulocytes, per cent. When there is no urgency the administration of iron is followed by attainment of equal and normal blood levels in three weeks or less.

SUMMARY

In 80 infants and children with anemia resulting from iron deficiency satisfactory therapeutic results were obtained when saccharated iron oxide in calculated dosage was given intravenously. The hemoglobin values were restored completely and rapidly in nearly every instance.

There were 66 infants and young children in whom iron-deficiency anemia was secondary to an inadequate intake of iron, with occasional other contributing etiologic factors. These infants showed a rapid rise from an initial mean hemoglobin level of 7.5 gm. per 100 ml. to 12.5 gm. The average daily rise in hemoglobin level was 0.156 gm. This was achieved with an average of two and two-fifths injections. The total average dose of saccharated iron oxide was 239 mg. There was little change in erythrocyte levels. Reticulocytosis became apparent by the second or

third day and reached its peak between the fifth and sixth days. The extent of the rise was inversely proportional to the initial hemoglobin level.

There were 14 infants and children in whom the anemia was associated with miscellaneous infections and related disturbances. The initial hemoglobin level in all cases was below 9 gm. per 100 ml. The mean rise in hemoglobin level was from 8 to 11.7 gm. per 100 ml., and the mean daily hemoglobin response was 0.126 gm. This was attained with an average of two and one-half injections representing 259 mg. of iron.

Of 198 intravenous injections, only 21 were followed by reactions. These were usually febrile. No reaction was severe enough to warrant the cessation of treatment.

It is concluded that when oral administration of iron is not effective or not tolerated, or when the parent's cooperation is not reliable, and when rapid and dependable regeneration of hemoglobin is desired, intravenous injection of saccharated iron oxide is a valuable addition to the methods of treating hypochromic anemia. Reactions are not more frequent than after blood transfusions and are usually less severe.

ULTIMATE RESIDUAL LESIONS OF ANTENATAL AND NEONATAL ASPHYXIA

Their Relation to Certain Degenerative Diseases of the Brain Appearing in Early Life

CYRIL B. COURVILLE, M.D.
LOS ANGELES

DURING the past century postmortem examinations of certain mentally deficient, spastic, or epileptic patients have frequently revealed unusual and bizarre gross alterations of the brain of obscure origin. It has been obvious that such lesions must have resulted from some pathologic process in early, perhaps even in intrauterine, life, but the nature of that process has remained the subject of much uncertainty and conjecture. The variable symptomatology usually manifested itself in infancy, at times in the period immediately following birth. The course was usually progressive, leading to death within a few months or years. At times, however, the patient survived for a considerable interval of time. The lesions exposed at autopsy presented such widely divergent structural alterations that, on the basis of these variances, the numerous students of the problem were inclined to construct an entire series of clinical entities. With the exception of true congenital malformations and degenerative disorders of definite genetic origin, these clinicopathologic complexes now constitute the major portion of the "diseases of unknown etiology" so far as the brain is concerned.

Some investigators have assumed that the lesions are congenital, possibly even genetic, because they have occurred in early infancy. However, they do not closely resemble the lesions of unequivocal congenital origin. A second group has considered them as infectious in character because in some instances microscopic study has revealed collections of lymphocytes in the meninges and in the brain. A third school has believed them to be of vascular origin because some of the lesions are reminiscent of certain residuals of impaired circulation. This conclusion is not too far afield from what now seem to be the facts in the case. Finally, a small group headed by Schwartz [1] concluded that birth injury was the chief causative factor, although no adequate explanation was offered as to the exact mechanism of production of the various lesions.[2] Although this last theory does not offer a com-

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Read before the Section on Psychiatry and Neurology, California Medical Association, Los Angeles, May 14, 1951.

From the Cajal Laboratory of Neuropathology, Los Angeles County Hospital, and the Section on Nervous Diseases (Neurology), College of Medical Evangelists.

1. Schwartz, P.: Die traumatischen Schädigungen des Zentralnervensystems durch die Geburt: Anatomische Unterschungen, Ergebn. inn. Med. u. Kinderh. **31**:165-372, 1927.

2. The differentiation between the effects of birth trauma and neonatal anoxia is too involved to be undertaken here. I have discussed this in some detail in a longer study (Courville, C. B.: Contributions to the Study of Cerebral Anoxia, Bull. Los Angeles Neurol. Soc. **15**:99-195 [Sept.] 1950).

pletely satisfactory solution to the problem, it should be emphasized that the traumatic factor was, in fact, closely allied to what now seems to be the actual cause.

I propose to review this group of diseases with the purpose of pointing out their specific and characteristic lesions and analyzing them in the light of what is known concerning a more recently investigated pathologic state, viz., cerebral anoxia. I propose to show that cerebral anoxia is capable of producing a considerable variety of structural changes in the brain, and that these lesions constitute the essential characteristic in many of these so-called degenerative diseases. In those occasional instances in which the connection is not so clear-cut, furthermore, the association of other telltale lesions makes this assumption quite logical.

Before one can draw even this tentative conclusion, however, it is necessary to investigate briefly the effects of oxygen-want on the brain. I shall therefore outline briefly the various changes in the brain which can follow exposure of the adult human being to lowered oxygen tensions.

EFFECTS OF ASPHYXIA ON THE BRAIN

It has been customary to think of the effects of anoxia on the brain in terms of its immediate consequences. Whether one examines the brain of a newborn infant who has been fatally asphyxiated or of an adult who has died within a few hours after cardiorespiratory failure following an inhalation anesthesia or exposure to carbon monoxide, the uniform finding is that of an advanced degree of congestion. In a fairly high percentage of cases, this congestion is associated with hemorrhages, either meningeal or central or both. Such findings may be present in the brain of persons who have survived for several days a severe anoxic episode.

In order to learn the essential residual effects of anoxia, it is necessary to make microscopic studies of the cerebral tissues. By examining the brains of persons who have survived for varying intervals, it is possible to construct a picture of the sequence of events which occurs in the course of survival and to secure thereby some basis for an understanding of the clinical syndromes resulting therefrom. In the first few hours of survival, e. g., after anoxia under nitrous oxide anesthesia, it is difficult to make out any alterations in the structure of the nerve cells which would indicate that anything unusual has happened. If the patient survives for a period of 24 to 36 hours, individual nerve cells or groups of cells may show loss of tigroid substance, may be pyknotic, or may begin to fade out of the picture. These changes become more evident between 36 to 48 hours, when groups of nerve cells in the cortex or corpus striatum (notably the globus pallidus) show evidence of physical degeneration, a change which is emphasized by the associated pallor of the area in which these groups of cells are found, by the enlargement of the pericellular spaces, and by a fenestrated appearance of the intervening interstitial tissues. After 48 hours these areas become larger and quite clear-cut, and consequently they now appear as areas of focal necrosis. These areas may be irregularly scattered throughout the cortex and corpus striatum, but in the former they tend to be grouped in series in one or more of the cortical cellular laminations (predominantly the third lamina). These individual foci ultimately fuse so that one or more laminar degenerations are to be found when three days have elapsed following the anoxic episode. These changes, if progressive, will result in focal scarring of the cortex or, in some instances, in widespread subtotal destruction of the cerebral cortex.

But this sequence of change does not occur in anoxia from all of the possible causes or clinical types. In almost all instances, however, the common denominator of anoxia is to be found in necrosis of some parts (usually the globus pallidus) of the corpus striatum.[3] Therefore, as subacute residuals of the various forms of severe anoxia with survival for periods of 6 to 12 weeks or even more, either focal scars or cyst formation in this structure is to be expected.

In order to understand the late residuals of anoxia, it is necessary to take note of the lesions which may be found consequent to anoxia of the various clinical forms. Those following prolonged exposure to carbon monoxide are particularly illuminating. Experimentally, there have been found such lesions as focal or widespread demyelination of the centrum or formation of central cysts.[4] In clinical cases with survival of four weeks or more, large areas of softening of the cortex and subcortex (incident to occlusion of some of the larger arteries)[5] and extensive nodular atrophy of the cerebral cortex[6] have been described. In other instances of long survival after nitrous oxide anesthesia, demyelination and cyst formation in the cerebral centrum have been observed.[7]

As a basis, therefore, for the investigation of the chronic residuals of neonatal anoxia on the one hand, and for the more specific analysis of certain chronic degenerative disorders of the brain in infancy or childhood on the other, we have available a number of proved lesions of anoxia: focal cortical necrosis and scarring; widespread diffuse as well as nodular atrophy of the cerebral cortex; alterations, both focal and diffuse, of the corpus striatum; areas of cortical and subcortical softening incident to arterial occlusion; demyelination of the centrum, and central cyst formation. Having established by these observations what anoxia can do, we are now in a position to inspect the various lesion-complexes which underlie some of the variable neurologic disorders of early life.

Because not all physical diseases of the brain of unknown origin can be attributed to the effects of anoxia before or during birth, it will be necessary to go over the rather long list of such diseases and select those which, by the nature of their characteristic lesions, or by the obvious anoxial nature of certain associated lesions, may be reasonably assumed to have this origin.

DEGENERATIVE DISORDERS OF THE BRAIN OF INFANCY AND CHILDHOOD

Since Cazauvieilh[8] in 1827 described a case of atrophy of one side of the brain, a wide variety of structural alterations in the brain during early life have been reported and rather critically analyzed. Because these lesions have differed so widely

3. Courville, C. B.: Cerebral Anoxia and Its Residuals, M. Arts & Sc. **1**:16-27, 35-44, 68-78 (April, July, Oct.) 1947; **2**:67-79 (April) 1948.

4. Yant, W. P., and others: Studies in Asphyxia, U. S. Public Health Bull. No. 211, Government Printing Office, 1934.

5. Footnotes 2 and 3.

6. Meyer, A.: Über die Wirkung der Kohlenoxydvergiftung auf das Zentralnervensystem, Ztschr. ges. Neurol. u. Psychiat. **100**:201-247, 1926.

7. Abbott, C. N., and Courville, C. B.: Degeneration of the Globus Pallidus After Nitrous Oxide Anesthesia: Case with Survival Period of 42 Days, Bull. Los Angeles Neurol. Soc. **3**:46-50 (March) 1938.

8. Cazauvieilh, J. B.: Recherches sur l'agénésie cerébrale et la paralysie congéniale, Arch. gén. méd. **14**:14, 1827; cited by Alpers, B. J., and Dear, R. B.: Hemiatrophy of the Brain, J. Nerv. & Ment. Dis. **89**:653-671 (May) 1939.

in their physical aspects, no one thus far has attempted to group them all under any one common causative mechanism. This is understandable, for it is difficult to understand what relationship could possibly exist, for example, between gross cortical atrophy on one hand and the peculiar disturbance in myelination characteristic of "status marmoratus" on the other. Before these apparent inconsistencies can be accounted for, however, the conditions to be considered should be listed. This present paper will be limited to a consideration of the following groups of diseases:

I. Diffuse cortical atrophies
   A. General cortical atrophies (including chronic progressive degeneration of the cerebral gray matter) [9]
   B. Cerebral hemiatrophy [10]
II. Sclerosing cortical diseases
   A. Widespread cortical sclerosis ("walnut brain")
   B. Lobar sclerosis of childhood (ulegyria; diffuse sclerotic type of Schob) [11]
   C. Local convolutional sclerosis (microgyria)
   D. Focal cortical scars and cysts
III. Diffuse atrophies of the corpus striatum (choreoathetosis; juvenile parkinsonism)
IV. Disorders of myelination (demyelination; hyperplasia of the myelin sheaths)
   A. Chronic generalized demyelinating states (encephalitis periaxialis diffusa,[12] including the acute infantile form [13] and the subacute form of childhood [14])
   B. Focal demyelinizing disorders of the basal ganglia (status dysmyelinisatus [15])
   C. Myelin hyperplasias affecting the cortex and the basal ganglia (status marmoratus; état marbré [15])
V. Cerebral cystic diseases
   A. Chronic cystic degeneration of infancy
   B. Gross cortical and central cyst formation (porencephaly)

I shall consider an analysis of only the four essential lesions which lie at the basis of these groups of structural disorders of the brain: (1) diffuse loss of nerve cells, either cortical or striatal; (2) the gross sclerosing processes which deform

9. Alpers, B. J.: Diffuse Progressive Degeneration of the Gray Matter of the Cerebrum, Arch. Neurol. & Psychiat. **25**:469-505 (March) 1931.

10. Mott, F. W., and Tredgold, A. F.: Hemiatrophy of the Brain and Its Results on the Cerebellum, Brain **23**:239-263, 1900.

11. Schob, F.: Pathologische Anatomie der Idiotie, in Bumke, O.: Handbuch der Geistes-Krankheiten, Berlin, Julius Springer **2**:779, 1930.

12. Schilder, P.: Zur Kenntnis der soggenannten diffusen Sclerose (Über Encephalitis periaxialis diffusa), Ztschr. ges. Neurol. u. Psychiat. **10**:1, 1912.

13. Krabbe, K.: Beitrag zur Kenntnis des Frühstadien der diffusen Hirnsklerose (die perivasculäre Marknekrose), Ztschr. ges. Neurol. u. Psychiat. **20**:108-115, 1913.

14. Scholtz, W: Klinische, pathologische-anatomische und erbbiologische Untersuchungen bei familiärer, diffuser Hirnsklerose im Kindesalter, Ztschr. ges. Neurol. u. Psychiat. **99**:651, 1925.

15. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen des striären Systems, J. Psychol. u. Neurol. **25**:661, 1920. The question arises whether the familial variety of this disorder (the so-called Hallervorden-Spatz syndrome) belongs in this category. In several of these disorders, two or more siblings of a family have sometimes been affected. Similar intrauterine disturbances in the fetal circulation in the case of consecutive pregnancies could explain this familial incidence. I have observed this association in three families, in only one of which the cause was suggested (bleeding during pregnancy had resulted in epilepsy and mental deficiency in twins, the result of a diffuse cerebral cortical atrophy).

the cortex generally or locally; (3) the disorders of myelination, either in the form of demyelination or hyperplasia, and (4) the formation of cysts in the cerebral centrum or cortex and centrum. I propose to show that similar lesions have been produced in postnatal life by some forms of asphyxia. It is first necessary, however, to define cerebral anoxia and to review briefly the mechanism by which it produces its effects on the central nervous organ.

ASPHYXIA AND THE MECHANISM OF ITS EFFECTS ON THE BRAIN

It has long been known that asphyxia, though not entirely selective in its effects on the brain, produces more damaging alterations in this structure because of the extreme sensitivity of nervous tissues to oxygen want. The resultant effects have been designated as cerebral anoxia. It has been pointed out in other studies that the tissues of the brain may be damaged to varying degrees by any of the types of anoxia: the stagnant, the anemic, the anoxic, and the histiotoxic forms.[5] If the ill effects on the central tissues were due alone to a decrease in oxygen tension in the blood, one would logically conclude that these effects would be more or less uniform and universal, but such is not the case. From one case to another one finds variable degrees of damage which is often sharply localized to given areas, given structures, certain cell laminations, or even to definite foci within these laminations. Some of this focalization is to be accounted for by the peculiar vascularization of such areas of the gray matter, and perhaps also by the special predisposition of certain types of nerve cells to oxygen-want.

However, some of these focalizing effects, particularly those which occur as a consequence of antenatal or neonatal anoxia, can be accounted for only on the basis of the action of anoxia on the function and structure of blood vessels. Unfortunately, these effects are still not completely understood, especially those incident to the more general aspects of the cerebral circulation in utero: It is not understood why these effects of circulation are limited in some instances to a single lobe or hemisphere, or why in other instances the entire brain is affected. A generalized atrophy can readily be explained by the diffuse effects of oxygen-want on the brain. It is also possible that a single major vessel or some of its branches may be altered structurally to give rise to lobar sclerosis or to the formation of porencephaly. But a hemispheral atrophy is to be accounted for most satisfactorily only by some effect on the carotid system on one side, possibly through a dysfunction of its vasomotor nerves. This opens up an entirely new field of investigation in the physiology of the cerebral circulation, a study essential to the comprehension of the larger aspects of antenatal and neonatal asphyxia.

DIFFUSE LOSS OF NERVE CELLS

In the diffuse cortical atrophies, whether acute or chronic, it is necessary to explain how the scattered cells are lost in order to account for the fact that the affected convolutions are simply reduced in size without any recognizable alteration in their internal architecture. Further analysis makes it clear that the atrophy of the entire brain, or cerebrum (Fig. 1*A*), or perhaps of only one hemisphere (Fig. 1*B*) (diffuse type of Schob)[11] is the result of a loss of nerve cells so diffuse that no obvious local changes in lamination have taken place yet so limited in degree that no disturbance in the interstitial elements has resulted. Certainly such effects

are not easily accounted for on the basis of an infectious process, for at present there is no known form of encephalitis capable of producing such changes. Nor can the situation be any more satisfactorily explained on the basis of a congenital anomaly, or even by a "birth injury" which has in some mysterious way selectively injured at random the numerous individual cellular elements.

The evidence for the diffuse effects of anoxia, so far as loss of nerve cells and general cortical atrophy is concerned, rests on a fairly secure experimental basis.

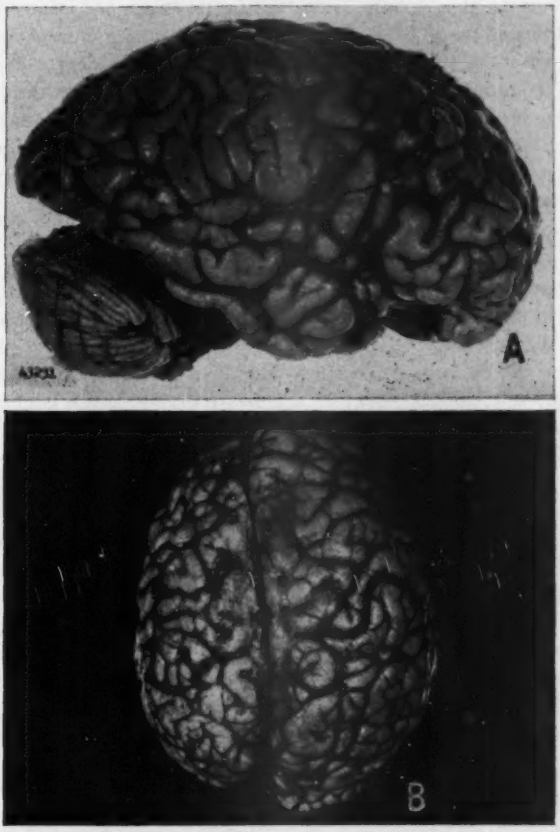

Fig. 1.—*A*, diffuse cerebral atrophy due to antenatal anoxia; generalized atrophy in a 22-year-old mental defective; vaginal bleeding between the fourth and fifth months of intrauterine life. *B*, diffuse cortical atrophy due to neonatal anoxia; cerebral hemiatrophy in a 22-year-old epileptic.

Windle, Becker, and Weil [16] recently conducted a series of experiments with pregnant guinea pigs and found that atrophy of the cortex, both general and local, not infrequently followed experimental anoxia in the offspring produced by temporary

16. Windle, W. F.; Becker, R. F., and Weil, A.: Alterations in Brain Structure After Asphyxiation at Birth: An Experimental Study in the Guinea Pig, J. Neuropath. & Exper. Neurol. **3**:224-238 (July) 1944.

occlusion of the uterine arteries. They found that this atrophy was due to generalized loss of groups of nerve cells in a cortex not otherwise damaged. These observations lead to the logical conclusion that one of the late effects of antenatal and neonatal anoxia is a more or less diffuse generalized hemispheral or localized atrophy of the brain.

A similar problem arises in regard to certain striatal disorders consequent to cellular rather than structural damage. Status dysmyelinatus [16] is accompanied by a gross shrinkage of the corpus striatum and allied structures and a loss of the myelinated fibers in the vicinity. Here again, however, as Denny-Brown [17] has pointed out, there is the gradual mergence of the resulting clinical syndrome with others which are more typical of anoxial origin. The high degree of susceptibility of the corpus striatum in particular to all forms of anoxia makes the assumption of the anoxial origin of this condition not too difficult to accept. The same holds true for progressive atrophy of the globus pallidus, seemingly responsible for the juvenile form of paralysis agitans, although the evidence in this case is not so definite and further study on this point is necessary.

CORTICAL SCLEROSIS, GENERALIZED OR LOCALIZED

It has already been established that one of the large groups of diseases of unknown origin in infancy and childhood is characterized by a generalized marked shrinkage of the cerebral convolutions (generalized cortical sclerosis or "walnut brain") (Fig. 2*A*), or by more localized alterations of this type (lobar atrophy of childhood [18] and microgyria) (Fig. 2*B*). The generalized form is characterized by an advanced state of diffuse atrophy and sclerosis of the cortex but a state in which the structural alterations are quite marked. In the localized form the changes are much more irregular and variable in degree. Such alterations have long been recognized by those familiar with lesions of the central nervous system, but here again the origin has been the subject of much conjecture. Theories as to possible causes have included arrest of development,[19] heredofamilial disorder,[20] ischemia,[21] meningeal hemorrhage [22] or other local vascular lesions,[23] or focal forms of encephalitis.[24] Such an array of hypotheses is not surprising, since the possibility of focal damage as a consequence of anoxia was not then known and since the ultimate focal sclerosing effects of this process were not appreciated. A further major obstacle to an understanding of these lesions was the fact that the very late effects of recognized clinical cases of anoxia were only rarely seen.

17. Denny-Brown, D.: Diseases of the Basal Ganglia and Subthalamic Nuclei, in Oxford Loose-Leaf Medicine, New York, Oxford University Press, 1946, pp. 261-302.

18. Friedman, A. P., and Courville, C. B.: Atrophic Lobar Sclerosis of Early Childhood (Ulegyria): Report of 2 Cases with Particular Reference to their Aspyhxial Etiology, Bull. Los Angeles Neurol. Soc. **6**:32-45 (March) 1945.

19. Collier, J. S.: The Pathogenesis of Cerebral Diplegia, Brain **22**:373, 1899; ibid. **47**:1-21 (Feb.) 1924.

20. Spatz, H.: Ulegyria, Zentralbl. ges. Neurol. u. Psychiat. **42**:121, 1926.

21. Bing, R.: Text-Book of Nervous Diseases, translated from German ed. 5 by W. Haymaker, St. Louis, C. V. Mosby Company, 1939.

22. McNutt, S. J.: Double Infantile Spastic Hemiplegia, Am. J. M. Sc. **89**:58, 1885.

23. Gowers, W. R.: Clinical Lectures on Birth Palsies, Lancet **1**:709 (April 14) 1888.

24. Long-Landry: La maladie de Little, étude anatomique et pathogenique, Paris, Thèse, 1912.

A clue to the situation, so far as the lesion itself is concerned, is found in the remarkable case reported by Meyer.[25] An autopsy done on a patient who had survived for 16 years a severe anoxic episode (carbon monoxide) revealed a peculiar nodular atrophy of the cerebral cortex. The similarity of this lesion to that of the

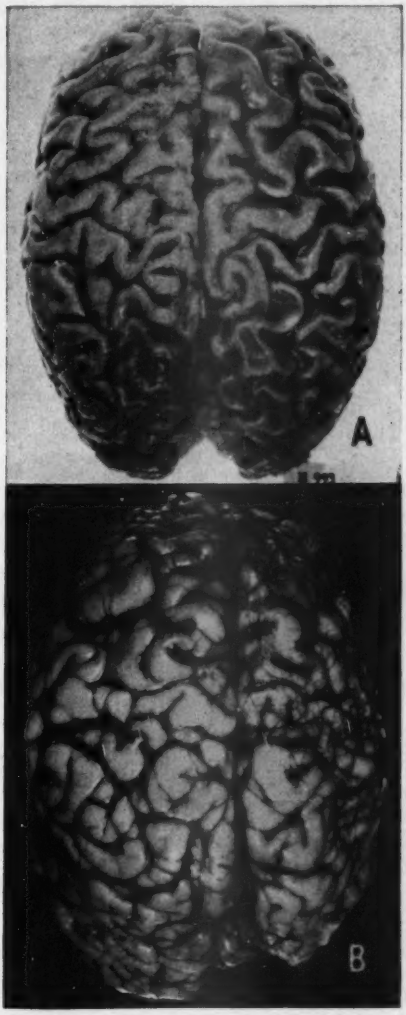

Fig. 2.—*A*, widespread cortical necrosis incident to diffuse partial anoxia; "walnut kernel brain." *B*, focal cortical sclerosis (ulegyria) incident to neonatal asphyxia; breech delivery after difficult labor of 36 hours; respiratory abnormalities for four days.

25. Courville, C. B.: Asphyxia as a Consequence of Nitrous Oxide Anesthesia, Medicine **15**:129-245 (Feb.) 1924; The Untoward Effects of Nitrous Oxide Anesthesia, with Particular Reference to Residual Neurologic and Psychiatric Manifestations, Mountain View, Calif., Pacific Press Publishing Association, 1939.

alterations found in the irregular atrophies characteristic of microgyria indicates that anoxia is capable of producing this type of cortical change. But even in acute cases, the irregular distribution of focal necrosis as observed in instances of cerebral anoxia following exposure to nitrous oxide[25] would indicate that an irregular atrophy of the cortex would be the ultimate residual if the survival period were

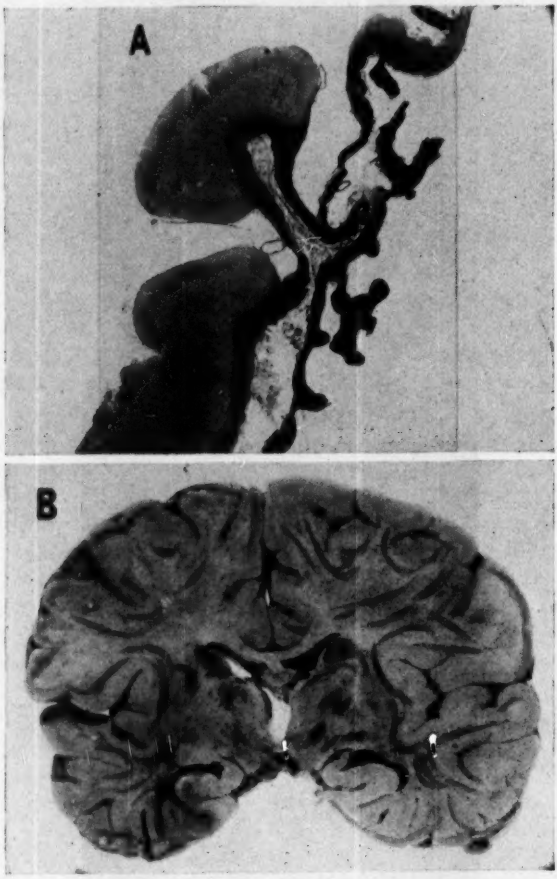

Fig. 3.—*A*, microgyria with formation of central cyst; premature infant born after rapid delivery and postnatal respiratory irregularities (Fig. 5 *B*). *B*, generalized demyelination due to "birth injury" (periaxial encephalitis, Schilder's disease); death at 9 years.

sufficiently long. Is it too much to conclude, then, that in the focal cortical scars which are so often the cause of epilepsy in early life, in microgyria (Fig. 3*A*) which is so often found in the pathologic complexes present in the brains of spastic persons (as in Little's disease, double hemiplegia, etc.), or in the shrunken cortex of lobar sclerosis of childhood (ulegyria) that anoxia is not only an adequate explanation of the presence of the lesion but also the best possible one?

DISORDERS OF MYELINATION AND CEREBRAL ANOXIA

None of the so-called degenerative diseases of infancy and childhood have been the subject of so much conjecture regarding etiology as have those characterized by the progressive disintegration of the myelin structures. In 1912 Schilder [12] introduced these diseases to medical science by collecting a group of representative cases from the literature and adding some examples of his own. To this condition he applied the term encephalitis periaxialis diffusa (Fig. 3*B*). Subsequent studies on this problem have suggested that a number of subtypes may be distinguished: (1) the acute infantile form,[13] (2) the subacute form of childhood,[14] (3) the adult form,[26] and (4) the chronic form which seems to have familial tendencies.[27]

The idea that the disease is an inflammatory one has been largely abandoned, most recent investigators [28] believing that it is the result of a disordered circulation. It is noteworthy that as far back as 1926 Grinker [29] called attention to the similarity between the changes characterizing this peculiar condition and those of demyelination following carbon monoxide poisoning. He then suggested anoxia as the possible cause. Since that time, it has become increasingly apparent that demyelination is a well-defined *late* residual of cerebral anoxia, not only after experimental anoxia [30] but also after anoxia incident to carbon monoxide [31] and nitrous oxide [32] in man. Is it not therefore quite possible that anoxia in utero or at the time of birth may be the actual cause at least of the acute infantile form and the subacute form of periaxial encephalitis (Schilder's disease) of childhood? Is there any other clearly understood mechanism which would furnish a better explanation for the condition?

The situation is not so precisely clear with respect to the excessive development of the myelin sheaths which constitutes the hallmark of status marmoratus,[15] otherwise known as état marbré, or marbling of the lenticular nucleus, of the thalamus (Fig. 4), and at times of the cerebral cortex. But even in these conditions, it has long been recognized that birth injury has so frequently been an important predis-

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26. Ferraro, A.: Familial Form of Encephalitis Periaxialis Diffusa, J. Nerv. & Ment. Dis. **66**:329, 479, and 616 (Oct., Nov., and Dec.) 1927.

27. Pelizaeus, E.: Über ein eigenthümliche Form spastischer Lähmung mit cerebralerscheinungen auf heredtärer Grundlage (Multiple Sklerose), Arch. Psychiat. **16**:698, 1885. Merzbacher, L.: Ein eigenartige familiär-hereditäre Erkrankungsform (Aplasia axialis extracorticalis congenita), Ztschr. Neurol. u. Psychiat. **3**:1, 1910. The matter of the familial occurrence of some of these diseases is too complex to be considered in this short paper. Nevertheless, it should not be forgotten that a peculiar intrauterine state in the same mother may explain this apparent familial, or possible genetic, factor. Some of my unpublished studies would seem to bear out this conclusion, but sufficient opportunity for study of this question has not yet been offered.

28. Wohlwill, F.: Über Encephalomyelitis bei Masern, Ztschr. Neurol. u. Psychiat. **112**:20, 1928. Marburg, O.: Hereditary Scleroses, Arch. Neurol. & Psychiat. **55**:338-352 (April) 1946.

29. Grinker, R. R.: Parkinsonism Following Carbon Monoxide Poisoning, J. Nerv. & Ment. Dis. **64**:18-28 (July) 1926.

30. Yant.[4] Morrison, L. R.: Histopathologic Effects of Anoxia on the Central Nervous System, Arch. Neurol. & Psychiat. **55**:1-34 (Jan.) 1946.

31. Hsü, Y. K., and Ch'Eng, Y. L.: Cerebral Subcortical Myelinopathy in Carbon Monoxide Poisoning, Brain **61**:384 (Dec.) 1938.

32. O'Brien, J. D., and Steegmann, A. T.: Severe Degeneration of the Brain Following Nitrous Oxide-Oxygen Anesthesia, Ann. Surg. **107**:486-491 (April) 1938.

posing factor that it cannot be entirely ignored.[33] In this connection it is interesting to note that Osler [34] once suggested that neonatal anoxia should be considered as a possible cause. Although we do not yet know the exact means by which this alteration occurs as a response to asphyxia at the time of birth, the frequent history of some untoward episode at the time of birth and the frequent association with other presumptive anoxial lesions, such as cerebral cysts and microgyria, make it more than likely that status marmoratus is a consequence of neonatal asphyxia. Nielsen [35] came to the same conclusion with respect to his case.

Fig. 4.—Status marmoratus (thalamus) in a case of dystonia musculorum deformans with symptoms since birth.

CYST FORMATION AS A CONSEQUENCE OF ASPHYXIA

There are two other cerebral lesions occurring in early life which have been the subject of much discussion as to their possible origin. Although both are alike in that the ultimate lesion is a cyst, the comparison ends at this point. In one of them, porencephaly, the cavitation is large and localized and is the obvious result of disintegration of both the cortex and centrum, while the other, chronic infantile cystic degeneration, is characterized by the formation of multiple cystic spaces in the

33. Norman, R. M.: État Marbré of the Corpus Striatum Following Birth Injury, J. Neurol., Neurosurg., & Psychiat. **10**: 12-25 (Feb.) 1947; État Marbré of Thalamus Following Birth Injury, Brain **72**:83-88 (March) 1949.

34. Osler, W.: The Cerebral Palsies of Children, Philadelphia, The Blakiston Company, 1889.

35. Nielsen, J. M.: Autopsy in a Case of Dystonia Musculorum Deformans, Bull. Los Angeles Neurol. Soc. **6**:87 (June) 1941.

cerebral centrum. Porencephaly has been variously considered as a congenital anomaly,[36] of inflammatory origin,[37] or of occlusion by thrombosis of an artery [38] or

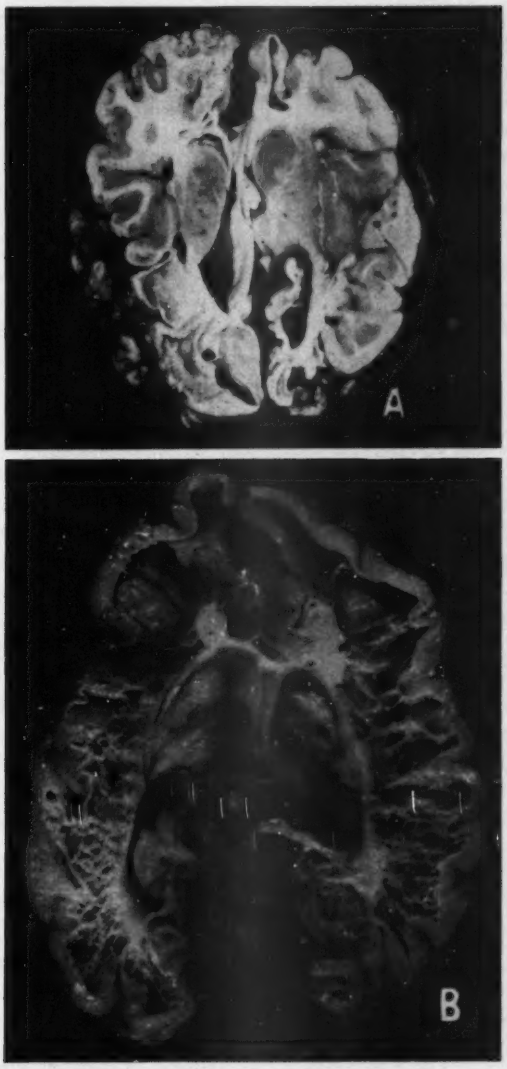

Fig. 5.—*A*, formation of porencephalic cysts in an infant of 3 years; severe asphyxia neonatorum with convulsions, spasticity, and ultimate dementia. *B*, Chronic cystic degeneration of infancy in a Negro infant aged 5 months; premature birth (7 months) with rapid delivery and postnatal respiratory irregularities.

36. Heschel, R.: Gehirndefect und Hydrocephalus, Vierteljahrsch. prakt. Heilk. **61**:59, 1859.

37. Strümpell, A.: Über die acute Encephalitis der Kinder (Polioencephalitis acuta, cerebrale Kinderlähmung), Jahrb. Kinderheilk. **22**:173, 1884.

38. Heubner, O.: Über cerebrale Kinderlähmung, Berlin Klin. Wchnschr. **19**:737, 1882.

of the cerebral veins.[39] In recent years it has been recognized that two types of this defect may occur[40]: the schizencephalies, believed to be developmental anomalies, and the encephaloclastic porencephalies. In the second group it has been postulated that, in some way, the artery supplying the affected area becomes occluded, resulting in softening and ultimate cyst formation (the ultimate result of phagocytic removal of the decadent material). Just how this arterial thrombosis occurs has not been made clear; but even though this mechanism proves to be the one responsible for the lesion, how does it fit into the scheme of neonatal anoxia? In instances of asphyxia following exposure to carbon monoxide with a survival period of a month or more, regional softening of the cortex and subcortex has been observed (Fig. 5*A*), especially in the parieto-occipital regions where porencephalic lesions are most commonly found. These softenings are apparently the consequence of thrombosis of the regional artery, resulting from a proliferation of the endothelial lining of the vessel.[41] Whether this is the sole factor or only one of the factors responsible in the case of neonatal anoxia, no one knows; but the history of some untoward episode at the time of delivery, and the frequent association of microgyria as a "label" lesion are more than presumptive evidence that asphyxia has something to do with its evolution.

The second cystic disease, chronic infantile cystic degeneration (Fig. 5*B*), has a long history, for the condition was first described by Virchow in 1867.[42] Although at first suspected of being of inflammatory origin, its early association with birth trauma was recognized,[43] and the assumption that such injuries were the actual cause was strengthened by its not uncommon association with subdural hematomas. As has already been pointed out, however, the distinction between true traumatic effects and those indicative of anoxia have usually not been clearly drawn in cases of difficult labor. It is therefore important to emphasize that the frequent association of the "label" lesions of microgyria and regional cortical atrophy with such cystic change suggests that intrauterine or neonatal anoxia is the ultimate cause. This idea is further supported by the fact that cystic degeneration of the cerebral centrum has been observed as a late residual of experimental asphyxia after cerebral anoxia from carbon monoxide[4] and nitrous oxide.[7] These observations further suggest that chronic infantile cystic degeneration in man and swayback in lambs may have a similar genesis.

GENERAL CONSIDERATIONS

In this very brief survey of the individual lesions which characterize a number of the degenerative diseases of the brain of infancy and childhood, an attempt has been made to marshall the evidence in favor of their anoxial origin. A summary

39. Marburg, O.; Rezek, P. R., and Marks, M. B.: Porencephaly: II. Studies in Phlebothrombosis and Phlebostasis, J. Neuropath. & Exper. Neurol. **4**:43-58 (Jan.) 1945.

40. Yakovlev, P. J., and Wadsworth, R. C.: Double Symmetrical Porencephaly (Schizencephalies), Tr. Am. Neurol. A. **67**:24-29, 1941.

41. Courville, C. B.: Pathology of the Central Nervous System: A Study Based upon a Survey of Lesions Found in a Series of 40,000 Autopsies, ed. 3, Mountain View, Calif., Pacific Press Publishing Association, 1950.

42. Virchow, R.: Zur pathologischen Anatomie des Gehirns, I. Congenitale Encephalities und Myelities, Virchow's Arch. path. Anat. **38**:129, 1867.

43. Sachs, B., and Peterson, F: A Study of Cerebral Palsies of Early Life Based Upon an Analysis of 150 Cases, J. Nerv. & Ment. Dis. **17**:295, 1890.

of this evidence follows. 1. In many instances of these various diseases there is a clear-cut history either of some abnormal intrauterine state, of some difficulty at delivery, or of the presence of certain postnatal symptoms which in themselves are strongly reminiscent of neonatal anoxia. 2. The occurrence of such diseases in early life suggests that the cause may be associated with intrauterine or natal states. 3. Individual lesions have been produced experimentally in animals, at times as a residual of asphyxia neonatorum. 4. Every lesion of the group (with the exception of status marmoratus) has been found as a consequence of asphyxia in postnatal life. 5. Lesions of more than one type are frequently associated, those of less certain origin together with those of unmistakable anoxial genesis. There is the added fact that most of these situations do not represent clear-cut, unequivocal clinical entities but rather shade off into an indefinite series of symptom-complexes produced by a variety of lesions in variable combinations which are found to be quite widely distributed in the brain. This further indicates that some generalized process, which may act in many different ways under variable circumstances, is the basic etiologic factor.

Why, then, has not all this been previously appreciated? Why has it taken a century or more to determine that such a kaleidoscopic variety of organic cerebral states may result from anoxia at birth? By way of answer, it should be remembered that medical science has been very slow to distinguish between the mechanical effects of trauma at birth on the one hand, and the chemical and physiologic effects of anoxia which so often accompany birth injuries on the other. In the second place, the pathology of anoxia in its various manifestations is a relatively recent product of neuropathology. While, to be sure, there have been in the past various theories as to the actual effects of anoxia, yet the total concept of diffuse loss of nerve cells in the cerebral cortex and corpus striatum, the sclerosing effects of focal necrosis, the late residuals of anoxia in the form of demyelination and cyst formation, and the secondary changes consequent to the occlusion of vessels following asphyxia have not been widely appreciated. Only when the ultimate residuals of asphyxia in its widest implications are fully understood can we apply our knowledge to the problem of diseases of unknown cause and thus clear up some of the mysteries as to the etiology of such diseases.

What is also important is that if neonatal anoxia is found to produce some of these characteristic physical lesions then further implications may be drawn as to the origin of some of the similar clinical states occurring in later life. If clinical anoxia is commonly characterized by the immediate occurrence of convulsive seizures, is it also the responsible factor in some cases of so-called idiopathic epilepsy, as Nielsen [44] has pointed out? If asphyxia may provoke a pronounced and prolonged psychoneurosis,[45] may some instances of intractable functional disorders have their genesis in minor and overlooked episodes of neonatal anoxia? May not many cases of low mentality and of behavior disorders [46] be likewise explained? If anoxia can produce

44. Nielsen, J. M.: Etiology of Idiopathic Epilepsy, Bull. Los Angeles Neurol. Soc. **11**:97-110 (Sept.-Dec.) 1946.

45. Fletcher, D. E.: Personality Disintegration Incident to Anoxia, Observations with Nitrous Oxide Anesthesia, J. Nerv. & Ment. Dis. **102**:392-403 (Oct.) 1945.

46. Preston, M. I.: Late Behavioral Aspects Found in Cases of Prenatal, Natal, and Postnatal Anoxia, J. Pediat. **26**:353-366 (April) 1945.

irreparable damage to the corpus striatum, may it not also injure its cellular constituents and account for some cases of juvenile parkinsonism or even parkinsonism of later life? If neonatal anoxia can produce lobar atrophy of infancy and childhood, may it not also be a factor in the later production of lobar sclerosis (Pick's disease) of adult life? If asphyxia neonatorum can produce the lesion of Little's disease, may it not also be ultimately responsible for the spastic paraplegias of adult life? But at present these questions all lie in the field of the hypothetical, a realm which should not be seriously invaded until it has been demonstrated that anoxia may initiate minimal functional changes in the nerve cell which render it incapable of living out its normal life span.

But in the case of even the well-defined structural entities, all the difficulties regarding their production have not been explained. There are yet many details of the problem which need illumination. My own studies have made it increasingly clear, for example, that many of these residuals are the result of antenatal anoxic states which can be explained only by some physical or physiologic disturbance of the fetal circulation. Bleeding during pregnancy or interruption of the placental circulation by infarction account for only a portion of these lesions. Other diseases of the placenta are also known to be responsible. It therefore becomes necessary to extend the search from the period of infancy and childhood into the intrauterine period. It will also be necessary to look into the abnormal physiologic states which leave a permanently and grossly damaged brain without any residual evidence as to why the damage occurred. These larger fields of study are now open for critical investigation.

1801 New Jersey Ave. (33).

Case Reports

TREATMENT OF DIAPHRAGMATIC HERNIA IN THE NEWBORN

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JAMES W. WEST, M.D.
AND
EDMUND G. LAWLER, M.D.
CHICAGO

EARLY recognition of diaphragmatic hernia in newborn infants and prompt treatment are responsible for the progressive lowering of the mortality rate associated with this developmental defect.[1] Whereas expectant treatment was more popular at one time, this practice has been abandoned in favor of early surgical corrective measures.

A consideration of the surgical treatment of this defect requires an understanding of the embryology involved.[2] The ventral division of the diaphragm takes its origin from the septum transversum, which divides the abdominal viscera from the heart. This septum migrates caudally from the neck region to a station at the level of the 12th rib. There is a union at this point of the thickened mesodermal cells of the dorsal mesentery. There is an opening which remains, however, in each posterolateral section of the diaphragm, the pleuroperitoneal canal, until the end of the fourth week, at which time a membrane from the pleura, superiorly, and a membrane from the peritoneum, inferiorly, cover these openings. Muscle fibers migrate between the two membranes to complete the muscular structure of the diaphragm. A failure in the fusion of the embryological components of the diaphragm results in openings between the pleural and peritoneal cavities and results in the hernias under discussion.

There are three sites for congenital diaphragmatic hernias:[3] 1. The pleuroperitoneal canal (foramen of Bochdalek) is the most common location, and hernias of this type usually occur on the left side. The liver tends to prevent hernias on the right side. This hernia is almost always without a sac. 2. Esophageal hiatus hernias occur owing to deficient hiatal circular muscle fibers in the diaphragm or to the congenital short esophagus which occurs with a portion of the stomach in the pleural cavity. The sac is present in this type of hernia. 3. Hernia in the retrosternal space (Morgagni's foramen) is a rare type. It usually possesses a sac.

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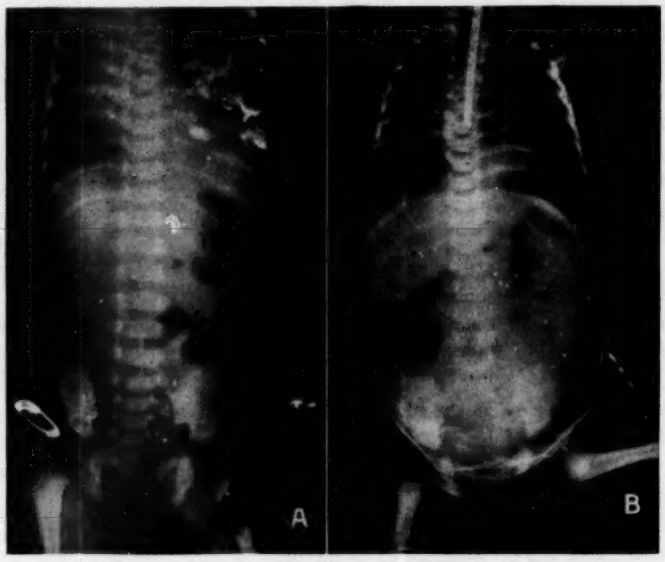
1. Blackwell, C. C.: Diaphragmatic Hernia in the Newborn, Am. Surg. **17**:638-648 (July) 1951.

2. Jordan, H. E., and Kindred, J. E.: The Diaphragm, in Textbook of Embryology, Ed. 4, New York, Appleton-Century-Crofts Company, Inc., 1942, p. 151.

3. Ladd, W. E., and Gross, R. E.: Congenital Diaphragmatic Hernia, New England J. Med. **223**:917 (Dec. 5) 1940.

The symptoms of congenital diaphragmatic hernia are present at birth. They manifest themselves as respiratory, circulatory, and digestive disturbances. The degree to which the cardiorespiratory system is embarrassed by displacement from the abdominal viscera will determine the severity of the condition. Usually cyanosis, especially during feeding, is a prominent sign. Rapid respiratory rate, rapid pulse rate, and shift of the apex beat to the right should make the clinician aware of the possibility of the condition. The diagnosis of diaphragmatic hernia is usually confirmed by the roentgenographic finding of gas-filled loops of bowel in the pleural cavity.

The treatment of congenital diaphragmatic hernia is early surgical intervention, inasmuch as this condition is rarely compatible with life. Preoperative care, includ-



A, preoperative roentgenogram; *B*, postoperative roentgenogram.

ing the passage of a Levin tube, with suction, blood transfusion during the procedure, and antibiotic therapy, is routinely used. The anesthesia should contain a high concentration of oxygen in a closed system, a tight fitting midget mask usually being sufficient.

Three types of approach have been used. The transthoracic approach is the best method in treating adult diaphragmatic hernias because of the adhesions usually present. The combined thoracoabdominal approach has been used in rare instances of pericardial involvement in the congenital hernias. The most commonly used and the best approach in children is the transabdominal method for two reasons: There are no adhesions present in diaphragmatic hernias in children, and prompt measures must usually be taken to replace the herniated viscera into the abdominal cavity. This usually involves undercutting the abdominal incision and closing the wound by means of the skin only. A layer closure, as a rule, is too tight and will cause cardio-

respiratory distress. Several months are required to allow the abdomen to enlarge sufficiently to accommodate the replaced viscera for a layer closure. The treatment is essentially one of converting a congenital diaphragmatic hernia into a ventral abdominal hernia which can be repaired at a later date. This two-stage method results in the lowest mortality rate.

REPORT OF A CASE

CASE 137080.—A newborn baby girl had a congenital diaphragmatic hernia through the pleuroperitoneal canal (foramen of Bochdalek). She presented the symptoms of cyanosis during feeding, rapid, shallow respiration, and rapid pulse rates. The apex beat was displaced to the right with active bowel sounds in the left chest. Physical examination revealed a poorly nourished white girl, 4 days old, who was cyanotic and dyspneic. The apex beat of the heart appeared to the right of the midline. Roentgenographic findings were confirmatory. Anteroposterior views revealed many loops of gas-filled intestine in the left pleural cavity. The mediastinum was markedly displaced to the right (Fig. 1*A*).

Therapy for this patient was early and prompt intervention through a transabdominal, left paramesial incision. The left pleuroperitoneal canal was located, and its margin determined. Air was permitted to enter the left pleural chamber by stretching the opening of the pleuroperitoneal canal, and the viscera were gently brought down into the abdominal cavity. The organs which had been herniated included the stomach, a portion of the duodenum (first part), the jejunum, the ileum, the cecum and the appendix, the transverse colon and a part of the left colon, the tail and the body of the pancreas, and the spleen. It was immediately obvious that the abdomen could not enclose these reduced viscera, and consequently the two-stage operation was decided upon. The diaphragmatic defect at the foramen of Bochdalek was closed, using size-00 Deknatel surgical silk, in two layers. The skin at the site of the transabdominal incision was undercut and closed with interrupted sutures.

The diaphragmatic hernia was thus converted to a ventral hernia. The postoperative course was uneventful. The roentgenographic findings following surgery show the mediastinum in the proper position and the left lung inflated to normal expansion (Fig. 1*B*).

SUMMARY

Embryology as it refers to congenital diaphragmatic hernia is discussed. The positions of the defects are located. The clinical picture is reviewed, and methods of treatment are outlined.

A case is reported, and the two-stage repair, which is the method associated with the lowest mortality, is described.

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RECURRENT EXTRADURAL CEREBELLAR HEMATOMA

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EXTRADURAL cerebellar hematoma is a condition not frequently encountered, and no report of recurrence of the condition with ultimate recovery has been found in the literature. Munslow [1] in a recent report stated that only seven cases had been found in which extradural hematomae occurring below the tentorium had been recognized and cured. The report of the following case, in which there was recurrence of hemorrhage and exacerbation of symptoms three days after relief by a first operation, seems justified.

REPORT OF CASE

Peggy S., aged 6 years, fell from a bed of average height to the floor, striking on her head. She was not unconscious and not believed to be seriously injured. Shortly afterward, however, she began to complain of headache, and the following day she was nauseated, vomited, and had considerable restlessness. On Jan. 6, 1946, three days after the accident, she was admitted to the Bluefield Sanitarium, and examination revealed a dull but cooperative 6-year-old girl with dilated pupils, who complained frequently of right frontal headache and some stiffness of the neck. There was marked fullness of the retinal veins, and the physiological cups were obliterated, but movements of the eyes and the visual fields were normal. Other cranial nerves were normal, and the reflexes were graded as follows: biceps, 2,2; triceps, 2,2; ulnar, 1,1; radial, 1,1; knee jerk, 0,0; ankle jerk, 1,1; plantar, both equivocal; abdominal, 2,2. Coordination of the arms was normal, and sensation was normal. A roentgenogram of the skull revealed a questionable subperiosteal fracture in the left occipital region. Laboratory tests showed a leucocytosis of 13,000 cells, a normal differential count, 88% hemoglobin, negative serologic reactions, and mild pyuria.

Since it was evident that there was increased intracranial pressure, bilateral upper occipital burr holes were made, and, when no extradural or subdural clot was encountered, a ventriculogram was done via the right lateral ventricle. The ventricular pressure was slightly increased, and roentgenograms revealed the ventricles in their normal position with air in each side, although only the right ventricle had been tapped. Following the ventriculogram, the child brightened, but 48 hours later she again showed signs of increasing intracranial pressure. On Jan. 8, 1946, with the patient under ether anesthesia, a midline suboccipital approach was made to the posterior fossa, and an extradural hemorrhage of the left posterior fossa was evacuated. The clot was large, nearly 1 oz. (28 gm.), and was evidently causing compression and a cerebrospinal-fluid block. No bleeding point was found. The child did well immediately following operation, and it was expected that she would continue to do well, but by Jan. 11 there was evidence of returned and increasing intracranial pressure, with bilateral papilledema and internal squint. Again the posterior fossa was exposed and the bone removed widely as for a classic suboccipital craniotomy. There was a second accumulation of clot on the left, beneath the muscle and higher up underneath the bone, apparently coming from a small leak in the

From the Department of Neurosurgery, Bluefield Sanitarium.

1. Munslow, R. A.: Extradural Cerebellar Hematomas, J. Neurosurg. 8:542-545 (Sept.) 1951.

lateral sinus, which had not been found before. All bleeding was stopped with crushed muscle; the dura was then opened, the cerebellar tonsils freed up, and the arachnoid opened to allow free escape of the cerebrospinal fluid and to determine free communication through the aqueduct. Following this operation the patient progressed favorably and was discharged from the hospital on Jan. 24. By April 13, 1946, Peggy was walking normally, her eyes were straight, with 20/30 vision, and her health was good.

She was not examined again until Aug. 18, 1951, when she came in at my request. She had grown to be a sturdy, healthy girl of 11, who reportedly had done well in school and behaved as other youngsters. Her vision was 20/20 in the left eye and 20/20—1 in the right eye; the visual fields were full and the fundi within normal limits. Station and gait, coordination, strength, and sensation were normal. She reported a little hearing difficulty, but the audiogram was normal. Tonsillectomy and adenoidectomy were recommended by the otolaryngologist to relieve Eustachian obstruction.

COMMENT

As no other similar case of recurrence of extradural cerebellar hemorrhage with recovery has been found in the literature, this case would seem to be unusual. Yet certain possible deductions seem justified. Since careful but unsuccessful search for a bleeding point was carried out at the first operation within the entire field of the clot, even to the left lateral sinus, it seems reasonable to conclude that the second bleeding was a true recurrence, rather than the result of an incomplete first operation. Jugular compression at the time of the first operation might have revealed the bleeding point. The enlargement of the bone opening at the second operation was done for assurance rather than of necessity. Opening the dura, freeing the cerebellar tonsils, and exposing the aqueduct after evacuating the second clot were deliberately carried out to insure complete relief of compression from the clot and to help reestablishment of the spinal-fluid circulation. I believe this was important.

SUMMARY

A case of recurrent extradural cerebellar hematoma with recovery has been presented. A five-year follow-up study has indicated satisfactory rehabilitation. Certain inferences regarding the case of this patient have been drawn.

CONGENITAL ABSENCE OF THE TIBIA

Report of a Case in a Negro Infant

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CONGENITAL absence of the tibia is a rare anomaly which is of interest to pediatricians and orthopedic surgeons. The cause is obscure. We wish to report this case in order to reemphasize the unsatisfactory and controversial status of the cause and management of the condition.

REPORT OF A CASE

R. F., a full-term Negro boy, was born at Freedmen's Hospital Oct. 24, 1950, weighing 2,723.5 gm. The delivery was normal and spontaneous, and the infant was in no distress at birth. Both parents were young and in good health. There was no history of trauma to the abdomen or exposure to x-rays during pregnancy, but the mother had experienced a moderate amount of vomiting and excessive fetal movements. Existence of similar deformities in other members of the family was denied. There were no siblings.

Upon physical examination the infant was found to be normal except for the deformity of the right lower extremity (Fig. 1). The right leg was adducted and flexed. Moreover, it was rotated to such a degree that the medial side looked upward and was distinctly concave and shorter than the lateral side. The deformed leg was 2.8 cm. shorter and was smaller in circumference than the left leg. The thighs were equal in circumference and length. There was a small depression on the lower lateral aspect of the right knee. The skin was intact over the entire right leg except for a small excoriated area resembling a pressure sore over the site of the prominent distal projection of the fibula which revealed on palpation a hard substance thought to be bone. It was evident from palpation that there was only one bone in the right leg. This lay near the lateral side of the right extremity; it extended from the depression below the knee to the excoriation at the distal part of the extremity and was apparently fibula. The external malleolus was easily palpable. The right leg dangled from an unstable knee joint which exhibited excessive lateral and rotary motion. The right foot was in extreme equinovarus position, and the sole of the foot faced directly forward. The digits were present and appeared normal.

The hemogram, the results of urinalysis, and the values for blood calcium, phosphorus, and alkaline phosphatase were all within normal limits. The reactions of the infant and parents to the Eagle serologic test were negative. Roentgenograms (Fig. 2) showed complete absence of the right tibia. The right fibula was 0.7 cm. shorter and 0.6 cm. narrower than the left, but otherwise it appeared normal in shape and contour. The proximal tibial center of ossification was absent on the right side. The left tibia and fibula appeared normal. There were two tarsal centers of ossification at each ankle. The other bones of the feet were present and appeared normal. No other gross abnormality of the skeleton was noted.

From the Department of Pediatrics of Howard University School of Medicine and the Pediatric Service of Freedmen's Hospital.

Fig. 1.—Photograph showing flexion, adduction, and rotation of the right leg which is shorter and smaller than the left. The right foot is in extreme equinovarus position, and the sole of the foot faces forward. The left lower extremity is normal.

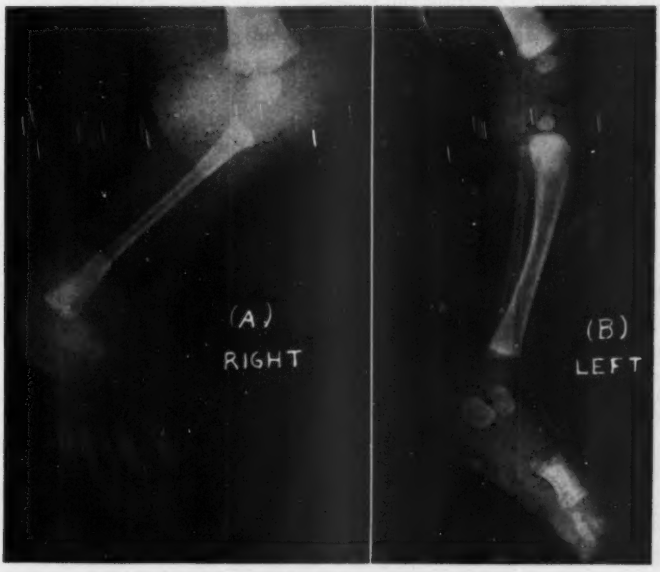

Fig. 2.—Roentgenograms showing (*A*) complete absence of the right tibia and proximal tibial center of ossification; (*B*) normal bones of the left leg.

COMMENT

The true cause of congenital absence of the tibia has not been ascertained. There are several theories of origin. These include (1) heredity, (2) endogenous or germinal origin, (3) fracture or trauma, (4) musculonervous origin, (5) nutrition, (6) amnion adhesions, and (7) virus origin.

Heredity seems to play a role in a number of cases.[1] Undoubtedly in some cases there is a strong familial tendency to bone defects. A variety of bone defects have been produced in mice by Bragg,[2] who states that abnormalities of the limbs are definitely inherited.

According to the endogenous or germinal theory,[1] absence or defect of the long bones is caused by a defective anlage of the skeleton. The complete or partial absence of a long bone is apparent evidence of the extent of the defect in the anlage. This hypothesis seems untenable, since it does not explain cases in which a rudimentary tibia is found represented by a fibrous cord, first described by McLaren[3] in 1889, or by cartilaginous nodules.[4] In these instances the anlage for bone was present, but the development was retarded.

The role of external violence occurring early in pregnancy with resulting fracture and resorption of bone has been considered. The fetus floats in a medium almost of its own specific gravity, is well surrounded by other organs, and is protected by uterine and abdominal walls. It is inconceivable that violence sufficient to interfere with growth or to fracture bones should not produce abortion.

It has been suggested[5] that under certain conditions of embryonal nervous excitation the limbs undergo violent convulsive movements which produce injury to the developing muscles and fracture the bones, with eventual destruction.

Warkany's[6] work is of interest in that it shows that the nutritional factor may play an important role in producing abnormalities in the skeleton. He fed rats a rachitogenic diet with supplementary vitamin D and obtained defects ranging from shortening to complete absence of the tibia in 51 out of 53 specimens examined. Defects of the tibia were the most frequent osseous anomaly encountered. It is questionable whether similar defects can be produced in the human fetus by dietary restriction or deprivation.

The theory most widely accepted is that defects in bone structure are due to pressure from bands and adhesions between the amnion and fetus or from pressure on the developing parts of the fetus by an amnion that is too small. According to this hypothesis,[5] the amnion suffers from external trauma or from an inflammatory process in early fetal life. Adhesions are formed in the region of the injured amnion,

1. Gaenslen, F. J.: Congenital Defects of the Tibia and Fibula, Am. J. Orthoped. Surg. **12**:453-481, 1914-1915.

2. Bragg, H. J.: Hereditary Abnormalities of the Limbs: Their Origin and Transmission, Am. J. Anat. **43**:167, 1929.

3. McLaren, J. S.: A Case of Congenital Absence of the Tibia, J. Anat. & Physiol. **23**:598-605, 1889.

4. Dankmeijer, J.: Congenital Absence of the Tibia, Anat. Rec. **62**:179-194, 1935.

5 Young, J. T.: The Etiology of Congenital Absence of the Tibia, Univ. Pennsylvania M. Bull. **18**:274-287, 1904-1905.

6. Warkany, J., and Nelson, R. C.: Skeletal Abnormalities in the Offspring of Rats Reared on Deficient Diets, Anat. Rec. **79**:83-94, 1941.

followed by acute polyhydramnios which causes the adhesive bands to exert traction on the extremity, pulling from their places the skin and underlying structures, thus isolating them and causing their absorption.[1]

Lewin [7] states that pressure from a small amnion exerted through the normal skin may cause ischemia of the deeper structures for a period sufficient to cause their death and complete disappearance or impairment of the viability to a point at which a rudimentary or defective limb results. Trauma, with the resulting decrease in amniotic fluid, must of necessity occur during the early weeks of pregnancy, for later the deficiency would cause a distortion of the skeletal parts rather than a disappearance of bones already formed.

Scars over the defective extremity are usually present and cicatrices have been described in other body areas.[1] In the case presented here, there was a scar at birth resembling a pressure area over the prominent distal end of the fibula on the affected limb.

The amniotic adhesion theory, although the most plausible, is nevertheless open to several objections. In cases where bone defects are bilateral,[8] there is usually perfect symmetry. It seems unlikely that adhesive bands could be so accurately placed as to cause a symmetrical duplication of the deformity in both limbs. Where there is a well-developed and normally directed fibula, as in the case presented here, it seems that pressure upon an extremity would not produce ischemia and absorption of one bone in the leg and leave the other relatively normal with no evidence of pressure. In several instances [1] there was no history of prenatal disease or trauma, and no abnormality of the amnion was noted.

It has been observed that there is a correlation between maternal rubella and malformations in the offspring.[9] Cataract and other ocular anomalies, as well as hypospadias, cleft palate, spina bifida occulta, and talipes equinovarus, have been reported in infants following maternal rubella during early pregnancy. Possibly defects of the long bones could be the result of prenatal viral infections that were not noticed or diagnosed. It seems as if no one theory explains all the conditions found.

Other abnormalities are usually associated with congenital absence of the tibia such as hypospadias, cleft palate, congenital dislocation of the hip, atresia ani, polydactylia, and syndactylia. The most frequent associated abnormality found, however, is talipes equinovarus. Young [5] suggests that the absence of the lower end of the tibia or internal malleolus removes the fulcrum for the action of the flexors of the foot, permitting extension of the foot and contraction of the tendo achillis. The deficient internal malleolus removes the opposition of the adductors of the foot, and the member is consequently drawn into a marked varus position. Some degree of varus deformity is seen in each case of complete or partial absence of the tibia.

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7. Lewin, P.: Congenital Absence or Defects of Bones of the Extremities, Am. J. Roentgenol. **4**:431, 1917.

8. (*a*) Gaenslen.[1] (*b*) Congdon, R. T.: Congenital Absence of Both Tibiae, Treated by Bone Transplants, Northwest Med. **21**:214-17, 1922. (*c*) Davidson, H. J.: A Case of Congenital Deformity of the Hands, Supernumerary Toes and Absence of the Tibiae, Am. J. Roentgenol. **5**:434, 1918.

9. Beswick, R. C.; Werner, R., and Warkany, J.: Congenital Anomalies Following Maternal Rubella, Am. J. Dis. Child. **78**:334-348 (Sept.) 1949. Bass, M. H.: Fetal Defects Resulting from Illness of Pregnant Mothers: Virus Diseases, New York J. Med. **48**:1807-1813, 1948.

Dankmeijer [4] found that 77 cases of congenital absence of the tibia had been reported up to 1935, of which 21 were bilateral. It was observed 22 times in females and 35 times in males. Of the 56 unilateral cases the defect was seen 32 times on the right and 6 times on the left; the side was not mentioned in the remaining 18 cases. Gray [10] found 120 cases reported by 1948. One of us (R. B. S.) [11] described a case of congenital absence of the fibula in a Negro infant.

In the cases described in the literature, several striking similarities are noted in the history and in the position of the leg and foot. Usually the parents and near relatives had no similar deformity. The maternal health was uniformly good during pregnancy. Sex and race apparently are not predisposing factors.[7] The deformity usually has the following characteristics. The lower part of the limb is strongly adducted with the result that the medial side of the leg faces upward and is concave. The medial side is therefore much shorter than the lateral convex side. Usually only one bone is palpable in the leg. The defective limb is dwarfed. The foot is in equinovarus position of varying degrees. The form of the foot varies from absence of the great toe, polydactylia or syndactylia, to a normal foot.

Roentgenograms reveal complete or partial absence of the tibia. When a portion of the tibia is absent, it is usually the middle or lower part, the proximal portion tapering to a cone. The patella may be absent or situated in an abnormal place. The fibula may articulate with the external condyle of the femur or be displaced backward and up on the shaft of the femur.[8b] It may be bent, hyperplastic, defective, or normal as in this case. It is of interest that most cases of malformation of the tibia are associated with congenital abnormalities in other organs and congenital scars and dimples, which would lead one to suspect defects of bone. Anatomical examination of the lower leg reveals muscular abnormalities. As a rule, the tibialis muscles and flexor hallicus longus are absent,[4] and those present have usually lost their bony attachments. The muscles which are present show misplaced origins and insert into the region of the rudimentary tibia which is represented by a fibrous bundle with or without cartilaginous elements. The main blood vessels and nerves are usually normal, but the pathways of their branches are usually aberrant.

TREATMENT

Definitive treatment in these cases is controversial and is essentially the problem of the orthopedic surgeon. In general, attempts have been made to obtain stability of the affected extremity by the use of bone transplants,[8b] arthrodesis at the ankle joint,[12] and stabilization of the fibula with bone wedges.[1] The first attempt is to maintain the fibula in good relation with the femur by the use of casts or other appliances, and the foot is carried out of varus and down under the fibula. Later, by surgical procedures, the fibula is placed in relation with the astragalus, and an artificial knee joint formed with the fibula participating.[13] Gohn [14] used a metal

10. Gray, J. E.: Congenital Absence of the Tibia, Anat. Rec. **101**:265-273, 1948.

11. Scott, R. B.: Congenital Absence of the Fibula: Its Occurrence in a Premature Negro Infant, Am. J. Dis. Child. **61**:1037-1043 (May) 1941.

12. Myers, T. H.: Congenital Absence of Tibia: Transplantation of Head of Fibula: Arthodesis at the Ankle-Joint, Am. J. Orthoped. Surg. **3**:72-85, 1905.

13. Green, W. T.: Personal communication to the authors.

14. Gohn, G.: Metal Substitutes for Tibia in Children, Deutsche Ztschr. Chir. **171**:119-124, 1922; abstracted in J. A. M. A. **79**:690 (Aug. 19) 1922.

graft as a substitute for the tibia with poor results, and amputation had to be done finally. Some orthopedists feel that amputation is the best approach to this problem, as is intended in this case, but the optimum time of operation is open to question.[15]

Congdon [8b] found in one case that ossification can occur up to the third year if cartilage for the tibia is present. It has been found that ossification can occur under stimulation of use; thus it is desirable that the defective limb remain undisturbed as long as feasible. Prognosis for normal gait is poor. Usually after these operations the knee joint is stiff, and braces have to be worn in order to give added support to the unstable limb.

SUMMARY

A case of congenital absence of the tibia in a Negro infant is reported.
The theories of the origin of this rare anomaly are discussed.
Treatment is controversial and in general unsatisfactory.
Prognosis for normal locomotion is poor.

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Dr. James R. Gladden of the Division of Orthopedic Surgery, Freedmen's Hospital, examined this infant and gave helpful suggestions in the preparation of this report.

15. Gladden, J. R.: Personal communication to the authors.

Abstracts from Current Literature

Biochemistry; Bacteriology and Pathology

Effect of Temperature on Survival of Chick Embryos Infected Intravenously with Cryptococcus Neoformans (Torula Histolytica). Albert M. Kligman, A. Peter Crane, and Robert F. Norris, Am. J. M. Sc. **221**:273 (March) 1951.

Intravenous infection of chick embryos with Cryptococcus neoformans produces almost 100% mortality. Incubation at 39, 40, and 41 C. markedly increases the rate of survival. At 40 C. the organisms are completely destroyed in eight days. Fever therapy is a possible therapeutic adjunct in the treatment of humans with Cryptococcosis.

Henske, Omaha.

Isolation of Histoplasma Capsulatum and Allescheria Boydii from Soil. L. Ajello and L. D. Zeidberg, Science **113**:662 (June 8) 1951.

The authors report the isolation of a strain of Histoplasma capsulatum from soil samples taken in Williamson County, Tenn., an area in which 70% of the population have positive cutaneous reactions to histoplasmin. Of a total of 101 soil samples from this locality, only one revealed the presence of this organism, whereas Allescheria boydii was isolated on two occasions.

Forbes, Dallas, Texas.

The Complex Pathogenic Action of the Tubercle Bacillus in Regard to Its Biochemical Makeup. P. F. Armand-Delille, Presse méd. **58**:533 (May 13) 1950.

Tuberculosis can produce specialized degenerative lesions and also an allergic response within an organism, which may result in severe or even fatal congestive reactions. This double action has been studied for half a century, and isolation of the various components of the body of the bacillus has been accomplished. The lipids will produce the histological changes characteristic of tuberculosis, but they do not bring out an allergic response, and will not result in a positive skin reaction. The nucleoproteins effect no nodular reaction, and only tuberculin will elicit a positive skin reaction. The chemical nature of tuberculin is still unknown.

These observations will influence the use of antibiotics. In cases in which nodular degeneration is present, antibiotics are of no value, but when young bacilli are in the circulation, antibiotics are most efficient.

Daffinee, Melrose, Mass.

Metabolism; Infant Feeding; Milk and Other Foods

Isolation of a Crystalline Albumin from Milk. B. David Polis, H. W. Shmukler, and J. H. Custer, J. Biol. Chem. **187**:349 (Nov.) 1950.

The authors were able, by means of salt and alcohol fractionation, to isolate and prepare in crystalline form a bovine whey albumin. This protein, which makes up approximately 3 to 5% of the total protein in cow's milk, has many physical properties in common with bovine serum albumin. The properties measured were molecular weight, optical rotation, isoelectric point, and electrophoretic mobility. The authors conclude that the two albumins are probably identical.

Forbes, Dallas, Texas.

A Modern Concept of Breast Feeding. Milton I. Levine, J. Pediat. **38**:472 (April) 1951.

The ideal type of infant feeding is the one that gives the greatest mutual satisfaction to mother and child. Doctors should encourage breast feeding. Prenatal care should include attention to inverted or small nipples and assurance that breast feeding can be a happy and rewarding experience.

Mothers who have no strong attitudes against breast feeding should be encouraged to nurse. However, mothers who would rather not nurse and mothers who have varying degrees of fear

or antagonism to nursing should not be encouraged to do so. The final decision as to the type of feeding must be made by the mother herself. Whatever method a mother finally undertakes, there should be no sense of inadequacy or self-reproach, and she should receive every encouragement from her physician.

MACDONALD, Pittsburgh.

TOTAL BODY WATER IN CHILDREN. BENT J. FRILIS-HANSEN, MALCOLM HOLIDAY, THOMAS STAPLETON, and WILLIAM M. WALLACE, Pediatrics **7**:321 (March) 1951.

Total body water was determined in 24 normal infants and children by means of deuterium oxide and simultaneous antipyrine dilution. Good agreement between the two methods was found. A micromodification of the antipyrine method was described. Total body water was found to be highest in premature and newborn infants, the values ranging from 70 to 80% of body weight. A gradual decrease in total body water, expressed as per cent of body weight, occurred during the first six months of life. From 6 months to 11 years, total body water was found to vary between 53 and 63% of body weight. It was pointed out that when considering any one particular case and comparing changes in body water in that case actual amounts of body water are a more useful mode of expression than per cent of body weight. This follows from the fact that significant changes in the absolute amount of water in the body reflect only small changes in terms of body-water concentration.

FROM THE AUTHORS' SUMMARY.

THE PERCUTANEOUS ABSORPTION OF WATER. ALINA S. SZCZESNIAK, HENRY SHERMAN, and ROBERT S. HARRIS, Science **113**:293 (March 16) 1951.

Using deuterium as a tracer, the authors were able to show that young male rats absorbed water when immersed for six to seven hours in a mixture of water and deuterium oxide. Shaving the rats did not influence the uptake of deuterium. Measurable quantities of deuterium were found in the heart's blood and in an additional series of rats in whom only the tail was immersed. The authors' data are not sufficient to permit calculations as to the cutaneous exchange rates.

FORBES, Dallas, Texas.

MANAGEMENT OF MARASMUS. D. N. MUKHEJEE, J. Indian M. A. **20**:312 (June) 1951.

The physiological principles of infant nutrition and changes in the marasmic state are discussed. Treatment is discussed from the physiological viewpoint.

McGUIGAN, Evanston, Ill.

AMINO ACIDS: I. METABOLISM AND PHYSIOLOGIC SIGNIFICANCE; II. AMINO ACID DETERMINATIONS IN BLOOD AND URINE. KURT SCHREIER and HANS PLÜCKTHUN, Ztschr. Kinderh. **68**:480 (No. 5) 1950.

The authors describe the metabolism and physiologic significance of 14 amino acids. Their method of serum-level determination of amino acids is reported in detail, and the serum levels are given for adults, children, infants, and premature infants. The urine values of amino acids in 24 hours for a 12-year-old child, six infants, and four premature infants are reported and detailed studies made on the influence of protein content of the diet on the amino acid elimination in two children and two infants. The addition of acid hydrolysate to the diet of two children resulted in an increase in the amino acid elimination in urine, and the authors feel that such studies of the contents of various amino acids in the urine permit a conclusion as to the amino acid value of a given hydrolysate.

GLASER, Jerusalem, Israel.

"PELENTAN SUBSTANCES" IN BREAST MILK AND THEIR PARADOXICAL INFLUENCE ON PROTHROMBIN. R. GOSTOI, J. HOMOLKA, and K. ZELENKA, Pediat. listy **5**:225 (April) 1950.

The influence of "pelentan substance" was studied in 42 newborn and premature babies. The "pelentan substances" curve in the blood of nursing mothers was found to differ from the curve in other people and there is proof that excreted "pelentan substances" are in breast milk in quantities of 3 to 6 mg. per 100 cc. after "pelentan" has been administered to the mother.

The presence of "pelentan substances" in the blood of breast-fed infants is demonstrated, and a higher frequency of hemorrhages is found among those children as compared with the frequency in hemorrhagic disease of the newborn.

Experimental proof is given that the "pelentan substances" eliminated in breast milk are not identical with tromexan "pelentan," (an anticoagulant of bishydroxycoumarin-like action); on the contrary, it stimulates the production of prothrombin.

It is shown that the lowering of the capillary resistance due to the "pelentan substances" effects bleedings only in places where the vessel was already injured and irrespective of the prothrombin level. The identity of the substance was not ascertained, and it is recommended that there be investigation of its eventual use as a substance with vitamin-K-like effect.

FROM THE AUTHORS' SUMMARY.

DISCUSSION ON VITAMIN-D MILK AND HOMOGENIZED MILK. U. HJÄRNE, E. ABRAMSON, G. FISCHER, O. MELLANDER, H. RONGE, A. LICHTENSTEIN, A. WALLGREN, and B. VAHLQUIST, Svenska läk-tidning. **47**:1213 (May 26) 1950.

The Stockholm Dairy Company had produced homogenized milk enriched with 450 units of vitamin D per liter and issued propaganda for its use. At a special meeting the Swedish Pediatric Society discussed the problem, and the opinion was generally expressed that, although not exactly necessary, this vitamin-D-enriched milk was an advancement in milk production. It was emphasized, however, that routine administration of vitamin D to all infants and small children supervised by the welfare centers should continue, even though these children were given vitamin-D milk, since the vitamin-D content was regarded as inadequate in the amount of milk usually given.

WALLGREN, Stockholm, Sweden.

FAT-TOLERANCE INVESTIGATIONS. YMKJE M. TRAP, Maandschr. kindergeneesk. **19**:181 (Aug.) 1951.

A study was made to determine whether influences on fat tolerance, which can be found in children with celiac disease, are evident in normal children as well. Although the limited scope of the observations permit no definite conclusions, the following tentative conclusions were made.

1. The fat tolerances in normal children diverge just as much as those in children with celiac disease. 2. The variance in the fat numbers can be large in children with a low fat output as well as in patients with a high one, which suggests that the condition of the child is only slightly responsible for this variance. 3. Even when they are in good condition, patients with celiac disease tend to have a lower fat tolerance than normal children, though in individual cases the tolerance can be extremely high. 4. The tolerance for the unsaturated part of the butterfat is better than that for the saturated part, not only in case of steatorrhea, but in normal children as well. 5. Decrease of the fat tolerance under the influence of wheat is possible, not only in children with celiac disease but also in those who, according to their fat number, may be considered normal. 6. Influences on the fat tolerance affect the unsaturated part of the fat as much as the saturated part. 7. The influence of wheat does not always manifest itself in patients with celiac disease. 8. The annihilating influence of nicotinamide on the wheat factor could not be confirmed when an amount of 20 mg. per day was administered. 9. There is an indication that the fat in feces may be mainly fat excreted from the blood. 10. The fat tolerance in children with celiac disease differs only in degree, not in principle, from that in normal children.

FROM THE AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

VITAMIN D INTOXICATION. HUGH CHAPLIN JR., LINCOLN D. CLARK, and MARIAN W. ROPES, Am. J. M. Sc. **221**:369 (April) 1951.

The characteristics of the syndrome of hypervitaminosis D are described, and data available on over 100 cases from the literature are summarized. Seven additional cases seen at the Massachusetts General Hospital within the past three years are described in some detail, with emphasis

upon the findings of band keratitis and metastatic calcium cysts. The histology of these cysts is described, as well as the nature of the Ca/P ratio of their contents.

Current methods for treatment of the syndrome are described. In addition to the already-available evidence regarding the inefficiency of nonspecific therapeutic use of vitamin D, as in most of the conditions listed in this paper, special stress is laid upon the hazards of such therapy. If vitamin D is used in massive doses, it is pointed out that careful follow-up study is obligatory for the early detection of clinical and laboratory manifestations of intoxication.

HENSKE, Omaha.

THE METABOLISM OF 1-C^{14}-L-ASCORBIC ACID IN GUINEA PIGS. J. J. BURNS, H. B. BURCH, and C. J. KING, J. Biol. Chem. **191**:501 (Aug.) 1951.

The authors present the results of a study aimed at a clarification of the metabolic pathways followed by ascorbic acid. For this purpose radioactive carbon was incorporated into ascorbic acid, which was then given to guinea pigs, both orally and intraperitoneally. Over a period of 10 days it was found that 66% of the administered radioactive carbon was expired as carbon dioxide and that 22% was eliminated in the urine. About one-third of the radioactive carbon excreted in the urine was found to be in the form of calcium oxalate, indicating that oxalate is an end-product of ascorbic acid metabolism. No marked differences were found in the distribution of the radioactive ascorbic acid in the organs and tissues of normal and scorbutic guinea pigs. There was no detectable incorporation of radioactive carbon into liver glycogen, the chondroitin sulfate of cartilage, or the collagen fraction of skin.

FORBES, Dallas, Texas.

VITAMIN A STORES OF SUCKLINGS FOLLOWING ADMINISTRATION TO THE DAMS OF VITAMIN A IN OILY AND AQUEOUS MEDIA. ALBERT E. SOBEL and ABRAHAM A. ROSENBERG, J. Nutrition **42**:557 (Dec. 11) 1950.

Orally ingested vitamin A in an aqueous dispersion is more effectively transferred to milk and stored in the suckling than vitamin A in an oily solution.

FREDEEN, Kansas City, Mo.

THE FOLIC ACID AND VITAMIN B_{12} CONTENT OF THE MILK OF VARIOUS SPECIES. R. A. COLLINS, A. E. HARPER, M. SCHREIBER, and C. A. ELVEHJEM, J. Nutrition **43**:313 (Feb. 10) 1951.

The free folic acid and vitamin-B_{12} content of milk from cows, goats, sheep, rats, dogs, sows, horses, and humans was determined microbiologically. The mean folic acid level of the milk from all eight species was found to vary from 1 to 4 γ per liter. The colostrum of the cow and the goat was observed to be higher in both folic acid and vitamin B_{12} than the regular milk of these species. The average vitamin-B_{12} content of milk from the cows, sheep, and goats studied was 6.6, 1.4, and 0.12 γ per liter, respectively. Commercial cow's milk was found to contain 1.6 to 6.5 γ of vitamin B_{12} per liter. The mean folic acid and vitamin B_{12} content of the milk from five human subjects were found to be 0.71 and 0.41 γ per liter.

FREDEEN, Kansas City, Mo.

RELATIVE EFFECTIVENESS OF VITAMINS A AND D IN OIL AND IN WATER. R. C. ELLINGSON, F. G. MCDONALD, O. N. MASSENGALE, and W. M. COX JR., Pediatrics **8**:107 (July) 1951.

When very low doses (1, 2, 3, or 10 units daily) of vitamin A in aqueous, emulsified, and oily preparations were administered to vitamin-A-deficient rats, growth response and cure of xerophthalmia were identical at comparable intake levels. Since the effect of rapid absorption and large liver storage (as claimed for water-soluble preparations) might not be operative at these low daily doses, relatively small single doses (14 to 140 units) of vitamin A in the three preparations were administered to vitamin-A-deficient rats. There was no difference in the average gains in weight or survival times of comparable groups of rats.

When low doses of vitamin A were administered to vitamin-A-deficient rats, the liver storages were equal for the water and oil solutions at comparable dosage levels of 10, 20, and 40 units. At

higher dosages, the aqueous and emulsified preparations resulted in larger storage than the oil solution. The antirachitic effectiveness in rats of calciferol, activated 7-dehydrocholesterol, and a mixture of D vitamins, such as in fish liver oil, was the same, irrespective of whether the vitamin was dissolved in oil or dispersed in water.

The data are interpreted to mean that the rapid absorption and high liver storage, as observed when excessive doses of certain vitamin-A preparations are administered, do not determine effectiveness when such preparations are given at ordinary prophylactic or therapeutic levels. At such levels an equivalence in effectiveness for oily, aqueous, and emulsified preparations has been demonstrated.

FROM THE AUTHORS' SUMMARY.

RESPONSE TO ADRENOCORTICOTROPHIC HORMONE IN CLINICAL SCURVY. HENRY S. TREAGER, GEORGE J. GABUZDA, NORMAN ZAMCHECK, and CHARLES S. DAVIDSON, Proc. Soc. Exper. Biol & Med. **75**:517 (Nov.) 1950.

Each of five patients with clinical scurvy, ages 36 to 75, were studied metabolically, and ascorbic acid was withheld. The corticotropin (ACTH) test was done in all patients in the scorbutic stage and repeated in four patients after the administration of ascorbic acid. One patient died on the sixth day of the study. The blood eosinophile response to corticotropin was that expected of patients with normal adrenal function and did not change following treatment with ascorbic acid. The authors state that it may be postulated that ascorbic acid is not necessary for the various adrenal functions studied or else there was residual ascorbic acid in the adrenals of these patients.

HANSEN, Galveston, Texas.

THE INFLUENCE OF ASCORBIC ACID PRETREATMENT OF THE LEUCOCYTE RESPONSE OF RATS EXPOSED TO SUDDEN STRESS. HABEB BACCHUS and CHARLES A. TOOMPAS, Science **113**:*269* (March 9) 1951.

Since previous workers had shown that ascorbic acid prevents the adrenal hypertrophy seen in animals exposed to cold, the authors decided to study the role of ascorbic acid in adrenal physiology through observations of leucocyte counts. In control animals injection of epinephrine regularly caused a reduction in the eosinophile count; whereas, in those animals given 150 mg. of ascorbic acid six hours prior to epinephrine injection no fall in eosinophiles was observed; in fact, a definite eosinophilia was noted. Histological examination of the adrenal glands indicated depletion of steroids and ascorbic acid in the control animals given epinephrine, whereas the animals who were pretreated with ascorbic acid were free from such changes.

FORBES, Dallas, Texas.

ACTION OF SEX HORMONES (ESTROGENS AND ANDROGENS) IN THERAPY OF HUMAN RICKETS WITH SPECIAL REGARD TO INORGANIC CALCIUM-PHOSPHORUS RELATIONS IN THE BLOOD. GIOVANNI BOI, Ann. ital. pediat. **4**:141 (April) 1951.

The author, who had already studied the connection between thyroid functions and rachitism, now reports the results of his studies of the action of androgens and estrogens on rachitic subjects, chiefly the alterations of inorganic phosphoremia and calcemia. He gives some hints on the structural affinity of these hormones with vitamin D and mentions previous observations, chiefly experimental. He reports data obtained for both types of hormones on rachitic and nonrachitic subjects.

GRULEE, Evanston, Ill.

PROTEIN HYDROLYSATES AND RICKETS. E. G. SCHULTZE, Ztschr. Kinderh. **68**:575 (No. 6) 1950.

Calcium occurs in the blood serum as ionized calcium, as colloid (protein bound), and in a complex, absorbable, ultrafiltrable form. This last form seems to be a compound in which the calcium is linked to organic acids, probably amino acids. This led to the thought that amino acids may have a preventive or curative effect upon rickets. The author studied this possibility on rats as well as on human infants, and he came to the conclusion that neither acid hydrolysates nor enzyme hydrolysates of casein had any effect in the prevention or treatment of rickets.

GLASER, Jerusalem, Israel.

EXCRETION OF AMINO ACIDS IN THE URINE IN A PATIENT WITH SCURVY. J. H. P. JONXIS and S. K. WADMAN, Maandschr. kindergeneesk. **18**:251 (Jan.) 1950.

In a patient with vitamin-C deficiency, an increased amino acid concentration in the blood and urine was found. Besides many amino acids, the urine also contained amino acid conjugates and peptides. After administration of vitamin C the amino acid concentration of the blood decreased first, the excretion of amino nitrogen returning to the normal level only some days later. The authors discuss the possible causes of this disturbance.

FROM THE AUTHORS' SUMMARY.

ORAL MANIFESTATIONS IN 75 CASES OF VITAMIN-B-COMPLEX DEFICIENCY. D. AFONSKY, Chinese M. J. **67**:243 (May) 1949.

In a girls' school, where the menu contained no milk or eggs and almost no meat, the staple diet consisted of crude polished rice, bean curd, and local vegetables, with a predominance of Chinese cabbage, bean sprouts, sweet potato, and turnips. Turnip greens were not used. Seventy-five girls, 35.7% of the student body, showed signs of vitamin-B-complex deficiency.

The most common lingual manifestation was engorgement and hypertrophy of fungiform papillae, signs of the acute form of niacin deficiency, although signs of chronic aniacinosis with marked atrophy of the papillae were also seen. Angular stomatitis, characteristic of riboflavin deficiency, occurred in 9.6% of the cases. It is interesting that no active Vincent's infection was seen, despite the fact that the organisms were often recovered on smears.

Deficiencies in one of the factors of the vitamin B complex are often associated with deficiencies in other factors, although the deficiency in one may be more pronounced than in others. The oral symptoms of thiamine deficiency may be obscure, and there are many variations in the symptoms of riboflavin and niacin deficiency. Treatment should, therefore, include the use of all three factors. In this study niacinamide, riboflavin, and dried yeast were administered for 10 days. The beneficial results were striking.

MACDONALD, Pittsburgh.

Hygiene; Growth and Nutrition; Public Health

THE RELATION OF BIRTH WEIGHT TO PHYSICAL GROWTH: A STATISTICAL STUDY. R. S. ILLINGWORTH, C. C. HARVEY and G. H. JOWETT, Arch. Dis. Childhood **25**:380 (Dec.) 1950.

The weight, standing and sitting height, pelvic girth, and chest and calf circumference were measured in 238 children, 5 to 8 years old, of three birth-weight groups (5 lb. 8 oz. [2,500 gm.], or less; 7 lb. 2 oz. to 7 lb. 6 oz. [3,200 to 3,300 gm.]; and 8 lb. 8 oz. [3,900 gm.], or more), and these data were analyzed by statistical methods. In all measurements the children of the lowest birth-weight groups were smaller than those of the largest birth-weight group, the measurements of the children of average birth weight falling (in all cases except in sitting height) between the two. Most of these differences were of statistical significance.

KELLY, Milwaukee.

CHILD MORBIDITY DEMONSTRATED IN A GENERAL HOSPITAL. E. M. POULTON, Arch. Dis. Childhood **25**:392 (Dec.) 1950.

The sick rate of children has been studied by analyzing the admissions of children to a general hospital over a period of two years. The age incidence of the commoner diseases is described, the age and sex incidence of fractures, burns, and other injuries are mentioned briefly, and the frequency of their occurrence is approximately assessed.

KELLY, Milwaukee.

GROWTH AND DEVELOPMENT IN THE CHILD: ITS SCIENTIFIC AND CLINICAL VALUE. G. DE TONI, Acta pediat. españ. **9**:553 (May) 1951.

Studies were done on the growth and development of children at the Growth and Development Center of the Clinical Pediatric Department of the University of Genoa, Italy.

The methods used are described. The author gives the history of such studies in the United States, including studies in Iowa and California, at Harvard University, and by Gesell at Yale University. He also gives briefly an account of European studies.

The use and disadvantages of Wetzel grids are also discussed. At the Auxology Center at Genoa, a modified classification similar to but simpler than the Wetzel grid is used. There are eight groups in this classification. The author discusses the use of growth and development studies clinically, and he feels that not only pediatricians but also general practitioners could learn much from the use of such studies.

ALLEN, Santa Fe, N. M.

SOME CONSIDERATIONS OF NORMAL AND ABNORMAL BIOLOGICAL TYPES AMONG SCHOOL CHILDREN OF MADRID: PRELIMINARY NOTE ON 1,000 CHILDREN. E. CONDE GARGALLO, Acta pediat. españ. **9**:591 (May) 1951.

Gargollo presents a preliminary study on growth and development of 1,000 children in the schools of Madrid, Spain. There were 500 girls studied yearly from the age of 3 to 13 years, and the same number of boys from the age of 4 to 13 years. The constitutional biometric classification of Prende was used, and the work done parallels in most ways that done by de Toni at the Auxological Center at the University of Genoa. A larger number of students are to be included in further study in order to correct errors which may be found in the study of this small number.

ALLEN, Santa Fe, N. M.

INFANT NATALITY AND MORTALITY IN BOLIVIA. MANUEL MERCADO MONTERO, Bol. Inst. internac. am. protec. infancia **25**:113 (June) 1951.

The author concludes that the hygienic and sanitary conditions of Bolivia are excessively backward. The data analyzed referred to cities, and it is easy to imagine the conditions which may be found in rural areas, where the inhabitants do not have any available aid in this field. As long as birth and death registrations are not well organized in Bolivia, any statistical work will be of little efficacy. Nevertheless this study may be considered as a real and effective sample of the actual demographic condition of Bolivia.

GRULEE, Evanston, Ill.

VOLUNTARY ACKOWLEDGEMENT OF ILLEGITIMATE INFANTS BY MOTHERS AT THE PROVINCIAL INSTITUTE OF INFANCY AT SASSARI. G. A. PIANA, Ann. ital. pediat. **3**:558 (Dec.) 1950.

The author gives the data on the acknowledgment of illegitimate children by year, 1945 to 1949, in the foundling hospital of Sassari, Italy.

FROM THE AUTHOR'S SUMMARY.

CORRESPONDENCE COURSES FOR MOTHERS. E. G. KARMÁNOVA and B. RODMAN, Pediatria **2**:55 (March-April) 1951.

The authors describe the organization of correspondence courses for mothers, which began in 1930 and were taken over by the Department of Public Health Education and enlarged in 1944. At first the plan included a 16-lecture course in the following subjects: care of breast-fed infant; development of infant; rickets; dysentery; gastrointestinal symptoms in early childhood; care of child from 1 to 4 years; scarlatina; diphtheria; influenza, measles, and whooping cough; tuberculosis; prevention of accidents to children, and a few others.

Limited at first to 10,000, distribution increased to 100,000 in 1950. Many courses have been added since then. A local physician and a consulting clinic of the given region are required to be in charge and help mothers. Method of teaching differs in various localities. The course takes three to six months, depending upon mothers' circumstances and time available. The aim is to give systematic knowledge of care of children to mothers who are unable to attend lectures and discussions. Polls are conducted among mothers to attain newer and better methods of approach. In spite of general education, many mothers lacked the necessary fundamental knowledge of care and understanding of infants and children. It was observed that they had better understanding of the prophylaxis of gastrointestinal diseases than of general care. Their knowledge of rickets or how to prevent it was limited.

Mothers are asked to answer questions pertaining to their methods of study and the time consumed. It is of interest that, with rare exception, the outlined lectures are read not only by the mothers but by most adult members of the family and friends as well. The immediate

practical application of the knowledge gained is obvious from the answers received. Periodic examinations through questions and practical demonstrations are conducted by consulting centers in each town or village. Constant growth of correspondence courses for both parents and the duty of pediatricians to utilize the opportunity are stressed.

BODER, Los Angeles.

PRIMARY INFANT MORTALITY DURING AND AFTER THE WAR IN FLORENCE. ALESSANDRO BIEBER, Riv. clin. pediat. **49**:271 (April) 1951.

The author gives a review of infant mortality before, during, and after the war (1930 to 1949) in Florence, Italy.

FROM THE AUTHOR'S SUMMARY.

INFANT WELFARE WITHIN AND OUTSIDE AUSTRIA. H. CZERMAK, Wien. klin. Wchnschr. **63**:146 (Feb. 23) 1951.

Infant mortality in Austria over several periods is discussed and compared with that of other countries.

AMBERG, Rochester, Minn.

Prematurity and Congenital Deformities

A CASE OF TURNER'S SYNDROME. GUY C. CUNNINGHAM and JOHN F. HARLEY, J. Pediat. **38**:738 (June) 1951.

Turner's syndrome consists of a congenital webbing of the neck, a deformity of the elbow (cubitus valgus), and genital infantilism. Of the few reported cases, most have been in females. This patient, a 7-year-old boy, has the third reported instance of Turner's syndrome in a male.

MACDONALD, Pittsburgh.

INDWELLING POLYETHYLENE NASOGASTRIC TUBE FOR FEEDING PREMATURE INFANTS. S. ROYCE, C. TEPPER, W. WATSON, and R. DAY, Pediatrics **8**:79 (July) 1951.

Experiences with an indwelling polyethylene nasogastric tube in feeding 30 small premature infants for periods varying from 7 to 49 days have been described. The technic has the following advantages. 1. The interval between feedings may be shortened, if necessary, without any increase in the likelihood of esophageal irritation. 2. Feedings disturb the infant so little as to cause no fatigue. 3. Feeding can be accomplished so easily that less skill is demanded of the nurse.

Two of the 30 infants died, and each had an ulcer in the upper, anterior part of the esophagus. Similar ulcers were noted by Gruenwald and Marsh in 16.66% of 310 autopsies on infants. In two other infants a purulent rhinitis developed on the side of the tube. Each infant suffered from other seemingly unrelated infections at the time. Thrush was never noted. Occult blood was absent in the 50 stools obtained from 18 infants, as indicated by a negative guaiac test. Nine of the 10 infants weighing less than 1,000 gm. at birth survived, as did 15 of the 16 who weighed 1,000 to 1,499 gm.

A complete evaluation of esophageal irritation in tube feeding as compared with gavage feeding will require a more extended study. Results so far with the polyethylene tube lead the authors to believe it to be a better device for feeding premature infants than either the rubber gavage tube repeatedly inserted or the dropper.

FROM THE AUTHORS' SUMMARY.

EFFECTS OF ACTH IN PREMATURE INFANTS. W. A. SILVERMAN, R. L. DAY, and F. C. BLODI, Pediatrics **8**:177 (Aug.) 1951.

In an effort to inhibit the progress of the proliferative vascular changes in the early stages of retrolental fibroplasia, 19 premature infants were treated with corticotropin (ACTH). The age of the infants at the start of treatment ranged from 15 to 84 days. The hormone was given in courses of 9 to 27 days, with dosage varying from 1.7 to 20 mg. per kilogram of body weight per day. Five infants received second courses of corticotropin. Two patients died following completion of therapy.

Hyperirritability, ravenousness, tachycardia, papular skin eruption, pitting edema, regurgitation, postinjection pallor and facies of Cushing's syndrome appeared during the course of corticotropin administration. Intercurrent infections, which responded to antibacterial therapy, occurred during hormone treatment. The urinary output of formaldehydogenic steroids increased markedly under the influence of the drug.

The average daily weight gains of the treated infants, calculated for comparable periods before, during, and after treatment were 24.9, 9.3, and 42.7 gm. per day, respectively. Increased caloric increase during therapy failed to modify the inhibiting influence of corticotropin on daily weight gain. "Rebound" increase in the rate of daily gain was noted following cessation of therapy.

Measurements of the length of the fibula were obtained from serial roentgenograms at 3- and 4-day intervals in 12 of the 19 corticotropin-treated patients. Growth in length of the fibula was retarded during therapy, and rebound increase in the rate of growth in length of this bone was noted upon cessation of treatment. Serial measurements of the occipitofrontal circumference of the head revealed changes in rate of growth during and following therapy that paralleled the fibular measurements.

The physical growth of presumedly identical twins, only one of whom had received treatment, was compared. The differences between the two infants in their physical dimensions were of the same order at the age of 10 months as they had been before therapy.

FROM THE AUTHORS' SUMMARY.

CONGENITAL HEMIHYPERTROPHY WITH LYMPHANGIOMA. J. ALED WILLIAMS, Arch. Dis. Childhood **26**:158 (April) 1951.

Hemihypertrophy in a 6-year-old girl is reported, with notes on theories of origin and clinical features. This particular case was of interest in that it exhibited a complete hemilymphangiectasis, including hemimacroglossia, associated with a large lymphangioma on the back.

KELLY, Milwaukee.

A CASE OF GARGOYLISM. GEOFFREY C. DE CRESPIGNY, Clin. Rep. Adelaide Child. Hosp. **2**:15 (May-Nov.) 1951.

The literature is reviewed and a case of lipochondrodystrophy (gargoylism) presented in detail.

McGUIGAN, Evanston, Ill.

PANCREATIC ENZYMES IN PREMATURE INFANTS. RUTH GSCHWIND, Ann. pædiat. **175**:169 (July-Aug.) 1950.

In 56 pancreas glands from 38 premature and 18 mature babies the quantitative contents of lipase, diastase, and trypsin were examined. The investigation showed that the presence of lipase and diastase could frequently not be demonstrated in young premature babies and that the values in premature babies and in very young mature babies are very low in any case. Trypsin could be found in every case, but in the young premature infants it was mostly in very small amounts.

In order to characterize the proteolytic power, the author compared the product of enzyme activity and weight of the glands in the different weight classes. The product is called proteolytic number. This decreases with increasing immaturity, and it decreases considerably more than the protein requirements. This behavior supports the practice of adding amino acids to breast milk for the raising of very small premature babies.

In a full-term baby of 5 months with fibrocystic disease of the pancreas, a very small content of all three enzymes was found. No deviations in the enzyme content of the organ were found in intoxication.

FROM THE AUTHOR'S SUMMARY.

INTERSTITIAL PNEUMONIA IN THE PREMATURE. E. FREUDENBERG and W. TOBLER, Ann. pædiat. **175**:185 (July-Aug.) 1950.

Interstitial pneumonia of premature babies, with a mortality of 21.7% among the 707 cases observed in Switzerland from 1941 till the end of 1949, represents an important illness.

There is no doubt that full-term children may also be affected, but premature infants are attacked with such a preponderance that one is justified in calling the disease an affection of the premature child. Because there is much evidence of contagiousness, interstitial pneumonia must be considered an infectious disease, and a virus infection must be assumed because bacteria have never been found. There is no connection with the usual "cold" diseases, rhinitis, pharyngitis, and bronchitis, nor with enteritis.

Several clinical signs, among them hematological differences, distinguish interstitial pneumonia from other virus pneumonias. The reason may be that a different organism is responsible or that there is a different age-conditioned reaction of the child. The natural resistance of full-term infants and relatively older children emphasizes the constitutional conditions of the illness, among which the disappearance of the antibodies received at birth toward the end of the first trimenon (when the illness is most frequent) seems worth considering. Attempts at prophylaxis with human gamma globulin did not show results in support of this hypothesis. Treatment with aureomycin and chloramphenicol has been tried in a limited number of cases but has proved of doubtful value.

FROM THE AUTHORS' SUMMARY.

DANLOS-EHLER'S SYNDROME. E. ROSSI and H. ANGST, Helvet. pædiat. acta **6**:245 (June) 1951.

Five new cases of Danlos' syndrome are reported from the pediatric and dermatological departments of the University Hospital, Zurich, Switzerland. The disease should be classified with the multiple hereditary abnormalities affecting children. The classic syndrome includes cutis hyperelastica, abnormal range of movements of the joints in extension, poor resistance of the skin to trivial trauma, with a tendency to formation of atrophic scars and hematomas. To these signs and symptoms must be added degenerative stigmas and multiple deformities. Since variants of the multiple deformities are usually seen among members of the same family through different generations, it must be assumed that this is a hereditary condition which, according to the theories of Hanhart, is of the facultative dominant character. The authors suggest that Danlos' syndrome resembles the pterygium syndrome sufficiently closely that the former should be considered a forerunner of the latter.

GRULEE, Evanston, Ill.

ULTIMATE PROGNOSIS IN IMMATURITY, BASED ON 543 CASES. P. BRUSA and P. MENGHI, Minerva pediat. **3**:218 (April) 1951.

A study of 543 premature infants, born between 1935 and 1945, revealed that the somatic and mental development had reached normal in the great majority of cases. After the second year of life, the mortality rate of children born prematurely was no different from the rate of children born at term. The incidence of respiratory infections and of congenital syphilis was higher in children born prematurely than in children born at term.

HIGGINS, Boston.

PHANEROGENESIS OF PRIMORDIAL DWARFS. B. RUDDER and E. KIPPER, Ztschr. Kinderh. **68**:567 (No. 6) 1950.

The authors feel that primordial dwarfs are not the product of pathological hereditary factors but rather of physiological "small-growth factors" as a result of the tendency of selective marriage between people of small size. Four family trees are presented.

GLASER, Jerusalem, Israel.

FAT BALANCE IN PREMATURE INFANTS. R. GOSTOF and J. HOMOLKA, Pediat. listy **6**:29 (No. 1) 1951.

Fat-balance studies were performed on 20 premature babies. A short commentary on the dynamic concept of fat metabolism is outlined and shows that fecal fat is not only endogenous but also exogenous in origin. In these studies characteristic steatorrhea, dependent upon the

quality, the mode of administration, and, partly, the quantity of digested fat, was ascertained. The necessary quantity of fat in the food of premature infants was shown to be very small, and a food low in fat was shown to be not only without later sequelae but actually advantageous if fat-soluble vitamins were administered in sufficient quantity.

FROM THE AUTHORS' SUMMARY.

ORGANIZATION OF NEWBORN DEPARTMENTS: 8. CARE OF PREMATURE INFANTS. E. ELEFANT, Z. NEJEDLA, and I. VONDRAKOVA, Pediat. listy **6**:182 (No. 2) 1951.

The care given to premature infants by obstetricians and pediatricians after birth and during the first days of life is reported. They are cared for at special centers for premature infants or in separated rooms in obstetric departments.

GRULEE, Evanston, Ill.

HYPERTELEORISM WITH POLYDACTYLY, HYPERPHALANGY WITH SPATULATE DIGITS. D. P. R. KEIZER, Maandschr. kindergeneesk. **18**:373 (No. 10) 1950.

A girl 7 years old exhibited a heretofore unknown congenital malformation consisting in hypertelorism, hyperphalangism, polydactylism, and digiti spatulaformes.

FROM THE AUTHOR'S SUMMARY.

FAMILIAL, CONGENITAL NEUROECTODERMAL DYSPLASIA. W. H. H. TEGELAERS, Maandschr. kindergeneesk. **18**:376 (No. 10) 1950.

A description of a familial congenital neuroextodermal dysplasia, total alopecia, and palmar and plantar hyperkeratosis, in combination with disorders of the central nervous system, in four of five children of one family is presented.

FROM THE AUTHOR'S SUMMARY.

SPRENGEL'S DEFORMITY. F. Y. KHOO and C. L. KUO, Chinese M. J. **67**:214 (April) 1949.

The authors describe a case of bilateral Sprengel's deformity associated with multiple anomalies of the cervicodorsal spine and ribs. The patient also had bilateral retrobulbar neuritis of unexplained cause.

MACDONALD, Pittsburgh.

Newborn

ROENTGENOLOGICAL MANIFESTATIONS OF GASTRODUODENAL ULCERATION IN THE NEWBORN. LESLIE L. LEMAK, Am. J. Roentgenol. **66**:191 (Aug.) 1951.

Gastroduodenal ulceration in newborn infants is not common. The cause is unknown. Among the possible contributing factors are (1) circulatory disturbances of the gastrointestinal tract, (2) high gastric acidity, (3) trauma secondary to gavage, (4) sepsis, and (5) burns and marasmus. A high incidence of brain damage and prematurity was noted in association with gastroduodenal ulceration in the 18 cases presented. Four of the 18 cases were examined roentgenologically, and they demonstrated a gas-distended stomach, with little or no gas in the small bowel. If pyloric stenosis and pyloric atresia are excluded, this is indicative of gastroduodenal ulceration.

HODGSON, Rochester, Minn.

ROENTGEN CHANGES IN THE UPPER INTESTINAL TRACT FOLLOWING THE USE OF CALCIUM CHLORIDE IN NEONATAL TETANY. WENDELL C. HALL, Am. J. Roentgenol. **66**:204 (Aug.) 1951.

Administration of calcium chloride orally, even in small doses, as a method of treatment for neonatal tetany, may produce necrosis of the lining tissues of the stomach, duodenum, and jejunum. Secondary deposits of calcium in the walls of the stomach, duodenum, and jejunum, with cicatricial changes, may occur following the mucosal damage, and roentgenograms of the abdomen may reveal the calcification two weeks after administration of calcium chloride.

HODGSON, Rochester, Minn.

COMPULSORY ROOMING-IN IN THE WARD AND PRIVATE NEWBORN SERVICE AT DUKE HOSPITAL. ANGUS MCBRYDE, J. A. M. A. **145**:625 (March 3) 1951.

Without significant new equipment or expense the large nursery on the maternity floor at Duke Hospital, Durham, N. C., was discontinued, and rooming-in on a compulsory basis was tried for a period of three years. The infant was bathed and dressed in the delivery room and placed in a bassinet which was put at the mother's bedside immediately. The infant and the mother were watched closely for the first 24 hours, and then, under guidance, the mother took over the care of the infant if she wanted to. For the most part the nurses did both obstetric and pediatric nursing. At first there was some turmoil, but there were no resignations. The operating costs were less than when there was a large nursery.

KIMBALL, Evanston, Ill.

THE FUNCTION OF A RECOVERY NURSERY IN A LARGE MATERNITY HOSPITAL. ALLAN BLOXSOM, J. Pediat. **38**:618 (May) 1951.

Full-term infants sometimes manifest difficulties in the first 24 to 48 hours that require special nursing care. Bloxsom has solved the problem of special care for these infants by building a "recovery nursery" within the same hospital unit as the premature nurseries. By combining the physical plant of the recovery nursery and the premature nursery, he is able to provide enough population to stabilize the nursing personnel and to fill the available hospital space that could not be filled by either a premature or a recovery nursery alone. The advantages to the infants are obvious.

MACDONALD, Pittsburgh.

HEMOLYTIC DISEASE OF THE NEWBORN IN DIZYGOTIC TWINS: AN INTERESTING FAMILY HISTORY. JAMES J. KELLY and G. JAMES SHAFFER, J. Pediat. **38**:717 (June) 1951.

The authors report an instance of hemolytic disease of the newborn in dizygotic twins. In this family there were 12 full-term births. Five children are now living. They are Rh +, with the same blood grouping as the father. Six children have died with signs consistent with hemolytic disease of the newborn. One child, the first, apparently died of birth trauma. It is interesting that the surviving children were not the first born and that the deaths from hemolytic disease were not consecutive.

The twins reported here reacted differently to their exposure to the Rh antibody. The first twin was apparently in fair condition at birth. The red blood cell count and hemoglobin maintained adequate levels. The nucleated red blood cells, after an initial rise, gradually disappeared within 24 hours. He was not given transfusions. On the fourth hospital day he suddenly deteriorated in appearance. He died on the fifth day. The other twin, a few hours after birth, showed a marked drop in hemoglobin and red blood cell count and a rise in nucleated red blood cells. He was given an exchange transfusion six hours after birth. He survived.

MACDONALD, Pittsburgh.

SALMONELLA INFECTIONS OF THE NEWBORN INFANT. HAROLD C. EPSTEIN, ADOLF HOCHWALD, and ROSEMARY ASHE, J. Pediat. **38**:723 (June) 1951.

A severe epidemic of diarrhea broke out in a newborn nursery, affecting 18 of 34 exposed infants. The causative organism was finally identified as Salmonella sp. (Type Oranienburg). In the subsequent bacteriologic research, this organism was cultured from a bottle-warmer used in the nursery, and further search revealed the organism in the stools of an electrician who had repaired the bottle-warmer a few days prior to the outbreak. The infants in this epidemic were seriously ill. Administration of aureomycin in doses of 25 mg. per kilogram of body weight was ineffective. Three of these infants died.

In another epidemic, 8 of 33 exposed infants became infected. The organism, Salmonella sp. (Type Barielly), was traced to the mother of the first infant affected. The disease was mild, and all babies recovered. The use of aureomycin may have been effective in this second outbreak.

MACDONALD, Pittsburgh.

PULMONARY HYALINE MEMBRANES IN NEWBORN INFANTS. W. BLYSTAD, B. H. LANDING, and C. A. SMITH, Pediatrics **8**:5 (July) 1951.

The results of analysis of 509 consecutive autopsies on newborn or stillborn infants with regard to the occurrence of pulmonary hyaline membranes are presented. These membranes occurred most commonly in premature infants and in full-term infants with a history of some complication of pregnancy, labor, or delivery capable of causing intrauterine asphyxia. Analysis of the results of differential staining of these membranes indicates that they are not formed of degenerated airway epithelium. Experimental injection of human amniotic fluid into the tracheas of excised artificially ventilated animal lungs resulted in membranes similar to those seen in the humans. It is concluded that the pulmonary hyaline membranes seen in newborn infants are formed of amniotic fluid aspirated as a result of intrauterine asphyxia.

FROM THE AUTHORS' SUMMARY.

THE PLASMA POTASSIUM LEVEL IN THE NEWBORN. D. P. EARLE, H. BAKWIN, and D. HIRSCH, Proc. Soc. Exper. Biol. & Med. **76**:756 (April) 1951.

Nine samples of placental blood were obtained via a needle in the umbilical vein before the cord was severed. Blood also was obtained from the femoral vein or the superior longitudinal sinus of 15 young infants. Dried heparin was used to prevent clotting, and the plasma was separated. Specimens with more than a faint trace of hemolysis were discarded. Potassium measurements were made on an internal standard flame photometer with an error of less than 1%. The plasma potassium levels were only slightly above the mean normal for adults, and all but 2 of the 15 infants had values greater than the adult mean.

HANSEN, Galveston, Texas.

RED CELL AND PLASMA VOLUME IN NEWBORN INFANTS. P. L. MOLLISON, N. VEALL, and MARIE CUTBUSH, Arch. Dis. Childhood **25**:242 (Sept.) 1950.

Estimations were made of plasma volume or red blood cell volume in 53 newborn infants, of whom 38 were normal and 15 were affected with hemolytic disease of the newborn. In 38 infants both plasma volume and red blood cell volume were estimated.

In 34 normal infants the average plasma volume was 41.3 ml. per kilogram. Plasma volume was not independent of hematocrit but rose steadily throughout the venous hematocrit range of 66.2 to 37.0. In four infants with hematocrits between 17.9 and 21.2, plasma volume was disproportionately raised, but these infants were in cardiac failure.

Red blood cell volume was measured in 44 infants. The relationship between venous hematocrit and red blood cell volume was approximately linear when the venous hematocrit was below 55%. However, above this level the venous hematocrit did not rise proportionately to the true red blood cell volume.

The total blood volume of 28 normal newborn infants, calculated from measurements of plasma volume and red blood cell volume, was 84.7 ml. per kilogram. Theoretically, blood volume is expected to increase with venous hematocrit, but this relationship could not be demonstrated conclusively in the present cases.

KELLY, Milwaukee.

HAEMOPOIESIS AND SIDEROSIS IN THE FOETUS AND NEWBORN. F. A. LANGLEY, Arch. Dis. Childhood **26**:64 (Feb.) 1951.

Two types of hepatic hemopoietic recession are demonstrated: (*a*) an intrauterine type, most marked in the last weeks before birth, and (*b*) an extrauterine type which succeeded birth after a lag period of one to three days. Extrauterine atrophy was found to follow an approximately logarithmic law. The mean time of disappearance of hemopoietic tissue from the liver of full-term infants was about eight days after birth, and for infants born 8 to 13 weeks prematurely, 37.6 days.

Siderosis of the liver and spleen was present both in fetuses and in infants born alive. After the first three days of life the degree of siderosis rose progressively to a maximum in about two weeks; it remained at this level for some months.

The evidence given here suggests that the postnatal fall in the erythrocyte count is, in part, due to atrophy of erythropoietic tissue in the liver. Evidence from the literature suggests that the cells produced by hepatic erythropoiesis have different properties, such as size and life span, from those derived from bone marrow.

In the fetus and newborn infant iron brought to the liver is used in hemopoiesis. When hemopoiesis diminishes after birth, the iron accumulates, giving rise to siderosis. Some of the excess iron is probably removed and deposited in the spleen. KELLY, Milwaukee.

SUBCUTANEOUS FAT NECROSIS OF THE NEWBORN. A. HOLZEL, Arch. Dis. Childhood **26**:89 (Feb.) 1951.

The author reports three cases of fat necrosis in newborn infants and discusses various etiological factors. Anoxemia resulting from asphyxia is suggested as the most likely predisposing element. Fat necrosis of the newborn is regarded as an inflammation of the fat tissues, not limited to the subcutaneous panniculus adiposus. Points of similarity with Weber-Christian disease are stressed. KELLY, Milwaukee.

PHYSIOLOGICAL HYPERBILIRUBINEMIA IN THE NEWBORN AND THE RESERVOIR FUNCTION OF THE SPLEEN. Y. AKERREN, Arch. Dis. Childhood **26**:106 (April) 1951.

The onset of pulmonary respiration abolishes intrauterine hypoxemia. The demands upon the means of oxygen transport, that is, the erythrocytes and the hemoglobin, are fewer than before. An unusually large number of red blood corpuscles therefore accumulate in the blood reservoirs of the spleen. This is revealed in the swelling of the spleen, which is characteristic of the newborn period and which culminates on about the third day of life. An increased destruction of erythrocytes and hemoglobin begins, owing to the intimate connection between the reservoir and the hemolytic functions of the spleen, and this in its turn leads to an increase in the bilirubin content of the blood. KELLY, Milwaukee.

TWO CASES OF ATRESIA OF THE SMALL INTESTINE IN THE NEWBORN. A. E. STEVENS, Arch. Dis. Childhood **26**:166 (April) 1951.

Two cases of congenital complete atresia of the jejunum are reported. In one there was recovery after operation. KELLY, Milwaukee.

ANEURYSM OF THE DUCTUS ARTERIOSUS AND UMBILICAL HAEMORRHAGE IN THE NEWBORN. BERNARD LENNOX and DERMOD MACCARTHY, Arch. Dis. Childhood **26**:169 (April) 1951.

The case is reported of a premature baby who died of sudden umbilical hemorrhage on the 11th day of life. At necropsy a 10-mm. aneurysm of the ductus arteriosus was found. A septic arteritis of the hypogastric arteries was present and was the cause of the umbilical hemorrhage. A similar change was found in the wall of the ductus aneurysm and was attributed to septicemic spread of the same infection. KELLY, Milwaukee.

CONGENITAL AND NEONATAL THROMBOCYTOPENIC PURPURA. H. N. ROBSON and C. H. M. WALKER, Arch. Dis. Childhood **26**:183 (April) 1951.

A comprehensive survey of the literature revealed 52 reported cases of congenital or neonatal thrombocytopenia. Three further examples are reported. These cases have been critically reviewed and classified. KELLY, Milwaukee.

PROPHYLAXIS FOR HEMORRHAGE OF THE NEWBORN (HYPOPROTHROMBINEMIA): NEED FOR OBLIGATORY USE OF VITAMIN K. BERNARDO PEREZ MORENO, Acta pediat. españ. **8**:1033 (Sept.) 1950.

The author reviews the literature on hemorrhagic disease of the newborn. In all countries in which infant mortality has been reduced, the mortality of newborn infants remains high. Various authors have put the incidence of intracranial hemorrhage at 25 to 65%. The incidence

may be even higher, since many cases are undiagnosed, and the disease may result in encephalopathies if the child lives.

It is well known that the tendency to hemorrhage is higher in newborn infants, due to the low prothrombin content of the blood. Lack of vitamin K in the mother's diet is an important factor, but since the fat-soluble vitamin K is found naturally in food, it is not easily utilized by the baby; it does not penetrate the placenta well, and also the baby's delicate biliary system is not capable of using it. Of course, any lesion affecting maternal liver function, including the use of chloroform at delivery, may increase the liability to hemorrhage in the newborn infant.

The author describes the types of clinical practices likely to result in hemorrhages, but he says that all women in labor should be given water-soluble vitamin K, 20 mg. subcutaneously or intravenously. This is to be repeated if labor is prolonged. The baby should be given 10 mg. immediately after birth and 10 mg. the following day, by mouth. This procedure, if it were made obligatory, should reduce the mortality of newborn infants from 1 to 0.67% of the present figure.

ALLEN, Santa Fe, N. M.

BLEPHAROSTAT FOR NEWBORN INFANTS AND VERY YOUNG CHILDREN. ALFREDO ARRUGA FORGAS, Acta pediat. españ. **9**:727 (June) 1951.

In examining the eyegrounds of very young children, especially during streptomycin treatment for tuberculous meningitis and for the detection of retrolental fibroplasia, the use of this small and effective blepharostat is a great help. Illustrations showing the instrument open and closed and also in use in holding back a newborn infant's eyelids are included.

ALLEN, San Francisco.

FORMATION OF PLASMA PROTEINS IN THE HUMAN FETUS AND ITS RELATIONSHIP TO MATERNAL PLASMA PROTEINS DURING PREGNANCY. H. EWERBECK and H. E. LEVENS, Monatsschr. Kinderh. **98**:436 (Oct.) 1950.

Total proteins of the human fetus were found to rise from 1.55 gm. at three months' gestation to 6.5 gm. at birth. During the same period maternal levels fell from 7.18 to 6.1 gm. Proteins consisted almost entirely of albumin during early intrauterine life and fell to normal levels during the course of gestation. Alpha and beta globulins were low during fetal life, and at birth, while gamma globulin rose during gestation. At birth gamma globulin was sometimes twice the normal value. There were no characteristic changes in the level of alpha globulin in the mother; maternal beta- and gamma-globulin levels rose during pregnancy.

It was postulated that the physiological hydremia of pregnancy was responsible for the fall in maternal plasma proteins and that increased load on the liver during the last months of pregnancy explained the fall of albumin. Increased beta globulin may have had to do with increase in serum lipids during pregnancy. There may have been a connection between the increase in maternal gamma globulin and change in the state of immunity of the mother or the presence of latent liver damage. Transplacental passage of complete plasma proteins from mother to fetus seemed unlikely. The fetus itself formed globulin from early gestation on and formed albumin from the fourth month on. Since the gamma-globulin level of the embryo and newborn infant was far higher than that of the mother while the antibody titer of the infant was never higher than the maternal titer, it was assumed that gamma globulin represented only the carrier and not the antibodies themselves. Gamma globulin levels could not be considered an index of immunity. No qualitative connection between maternal and fetal plasma proteins could be established. Electrophoretic changes in the maternal protein levels seemed to have no influence on the fetus.

HARTENSTEIN, Milwaukee.

SUDDEN CYANOSIS IN NEWBORN INFANTS CAUSED BY ANILINE POISONING ORIGINATING FROM DYE USED FOR MARKING NAPKINS. K. WEIGL, HOLUB, and HOMOLKA, Pediat. listy **6**:111 (No. 2) 1951.

Cyanosis appeared in a large number of newborn infants as a result of a proved aniline poisoning produced by a dye used for marking napkins in hospitals and institutions.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF HEMOLYTIC DISEASE IN THE NEWBORN WITH EXCHANGE TRANSFUSION. BIRGER BROMAN, Svenska läk-tidning **46**:25 (Jan. 7) 1949.

Exchange transfusion should be performed within the first hours after birth. If delayed until the second day of life, it has no better effect than ordinary blood transfusion. On the other hand, it is often difficult to decide immediately after birth whether exchange transfusion is necessary, and much personal experience is required in order to make the decision. The author, therefore, recommends the centralization of this type of treatment, which should not be performed in county hospitals. Five cases of successful exchange transfusion in icterus gravis are reported.

WALLGREN, Stockholm, Sweden.

HYPOGLYCEMIA IN NEWBORN INFANTS OF DIABETIC MOTHERS. JOHAN RIIS, Tidsskr. norske lægefor. **70**:7 (Jan. 1) 1950.

Two cases are reported. One half-hour after birth both infants displayed cyanosis, paleness, and flaccidity. Tests showed hypoglycemia (20 mg. and 28 mg. per 100 cc., respectively). After intramuscular injection of dextrose, improvement was effected.

WALLGREN, Stockholm, Sweden.

ILEUS IN NEWBORN INFANTS. TYGE C. GERTZ, Ugesk. læger **112**:203 (Feb. 16) 1950.

Four cases of ileus, successfully operated upon during the first week of life, are reported. In the first case there was a typical meconium ileus that became symptom-free after injection into the small intestines of pancreatin. A relapse of the ileus, due to adhesions, occurred one month later and was also successfully treated surgically. In the second case there was an isolated atresia of the ileum. In the third case there was malrotation of the colon, with volvulus of the whole small intestine. In the last case there was stenosis at the duodenojejunal junction.

The diagnosis of ileus in newborn infants is discussed, and the importance of making regular roentgenograms of the adbodmen, combined with barium enema, is stressed. The value of biochemical examination of the duodenal juice in the diagnosis of meconium ileus and of microscopic examination of the meconium in the diagnosis of atresia is stressed.

WALLGREN, Stockholm, Sweden.

ACCIDENTS IN PROPHYLAXIS OF OPHTHALMIA NEONATORUM. SIE BOEN LIAN, Chinese M. J. **67**:328 (June) 1949.

The author points out that ophthalmia neonatorum may result from failure properly to instill 2% silver nitrate into the eye. Some physicians and midwives fail to get the solution into the conjunctival sac. The accidental use of stronger solutions of silver nitrate is fortunately rare but has occurred.

MACDONALD, Pittsburgh.

Acute Contagious Diseases

SECOND ATTACKS OF POLIOMYELITIS. ARCHIBALD L. HOYNE and IRVING LIPTON, J. A. M. A. **146**:707 (June 23) 1951.

The only authentic second attack of poliomyelitis with autopsy findings is that of a woman who contracted poliomyelitis with paralysis and atrophy of the left leg and then died in a second attack five years later. Autopsy findings showed complete demyelinization of the nerve fibers in the lumbar region on the left, which represented the old lesion, and anterior horn-cell degeneration and small round-cell infiltration widely dispersed, representing the recent lesion. The second attack was probably due to infection by a different strain.

KIMBALL, Evanston, Ill.

TONSILLECTOMY AND POLIOMYELITIS: II. STUDIES ON INCIDENCE IN 1949. MORRIS SIEGEL, MORRIS GREENBERG, and M. C. MAGEE, J. Pediat. **38**:537 (May) 1951.

From a detailed statistical study of 53,007 tonsillectomies performed in New York in 1949, the authors conclude that tonsillectomy predisposes to the development of clinical symptoms of poliomyelitis. Fifty cases of poliomyelitis were reported from this group. Most of the patients were under 10 years old. The most hazardous time for operation is April, May, and June, particularly June; the safest months for tonsillectomy in New York appear to be December, January, February, and March.

MACDONALD, Pittsburgh.

STATISTICAL ANALYSIS OF 242 CASES OF MENINGOCOCCUS MENINGITIS. BENJAMIN KAUFMAN, HAROLD LEVY, and BERNARD D. ZALEZNAK, J. Pediat. **38**:705 (June) 1951.

Sulfadiazine is the sulfonamide of choice in the treatment of meningococcus meningitis. When this drug was used alone results were superior to those obtained with combinations of the drug with other sulfonamides and with penicillin. The authors also observe that spinal puncture in these cases should be reserved for diagnostic purposes only.

MACDONALD, Pittsburgh.

MUMPS MYOCARDITIS. M. Z. IRVIN, T. H. BACHARACH, and ROSCOE L. PULLEN, Northwest Med. **50**:583 (Aug.) 1951.

The authors emphasize the possible development of acute myocarditis complicating mumps and appeal for a careful clinical study of every patient with parotid or other swelling thought to be mumps. Too frequently the convalescence of patients following apparent recovery from mumps or other acute infections is hurried, and the presence of accompanying myocarditis or other systemic involvement is overlooked.

Use of the complement-fixation test is discussed in the diagnosis of the systemic manifestations of mumps in the absence of parotitis. Atypical mumps with electrocardiographic evidence of myocarditis in a young man is described.

DOCTOR, Seattle.

ROLE OF HYALINE MEMBRANES, BLOOD, EXUDATE, EDEMA FLUID AND AMNIOTIC SAC CONTENTS IN PREVENTING EXPANSION OF THE LUNGS OF NEWBORN INFANTS. FRANKLIN C. BEHRLE, DAVID M. GIBSON, and HERBERT C. MILLER, Pediatrics **7**:782 (June) 1951.

The lungs of 43 infants were removed at autopsy and expanded with measured amounts of negative pressure. The amounts of pressure required to initiate expansion and to bring about apparent complete expansion of the gross specimens could not be correlated with the final degree of expansion that was obtained, as measured by the thickness of the alveolar walls. Expansibility of the lungs was impeded in two groups: those with a birth weight less than 1,200 gm. and those who had extensive hyaline membranes in the lungs. The presence of amniotic-sac contents, blood, exudate, and edema fluid in the alveoli and air passages, even in large amounts, did not mechanically prevent what appeared to be satisfactory expansion of the lungs.

FROM THE AUTHORS' SUMMARY.

ENCEPHALITIS COMPLICATING ATTENUATED RUBEOLA. J. L. ROSENZWEIG and W. G. KLUGH, Pediatrics **8**:85 (July) 1951.

A case of encephalitis complicating attenuated measles is presented. This is the first such case in the literature, and the authors suggest recordings of other such cases in order to evaluate better the total advantages of the use of human immune serum globulin.

FROM THE AUTHORS' SUMMARY.

MUMPS MENINGOENCEPHALITIS. LILLIAN P. KRAVIS, M. MICHAEL SIGEL, and GERTRUDE HENLE, Pediatrics **8**:204 (Aug.) 1951.

Eighty-five cases of meningoencephalitis were analyzed from a clinical and serologic standpoint, with greatest emphasis placed upon the serologic findings in the complement-fixation test. Clinical data were complete in 71 cases. Of these, 38 patients showed no signs of mumps-virus infection other than meningoencephalitis. Such widespread occurrence of meningoencephalitis as the sole manifestation of mumps-virus infection points up the value of a rapid, reliable, and specific laboratory test for the diagnosis of mumps. The complement-fixation test employing the soluble and viral mumps antigens was evaluated with the above criteria in mind.

Of the total group of 85 patients, 62 showed definite serologic evidence of infection with mumps virus. In 43 of these, the first serum had antibodies against the mumps-soluble antigen in higher titer than those against the mumps-viral antigen (anti-S > anti-V pattern), thus demonstrating a pattern of antibody response found to be typical of early mumps infection. In the remaining 19 of the 62 cases, a positive diagnosis was based on the demonstration of a rise in both types of antibodies.

Twenty-three of the total of 85 cases showed suggestive serologic evidence of mumps by virtue of high initial antibody levels. A large number of patients in the latter category had parotitis preceding or concomitant with meningoencephalitis.

The anti-S > anti-V pattern occurs most frequently when the meningoencephalitis is not preceded by salivary gland involvement and when the serum is obtained before the end of the first week of illness. Under proper conditions, early serologic diagnosis is possible in about two-thirds of cases of mumps meningoencephalitis without preceding or concurrent salivary gland involvement.

The clinical findings and routine laboratory data on spinal fluids and bloods in this study are in accord with those previously reported by others.

FROM THE AUTHORS' SUMMARY.

POLIOMYELITIS AND COXSACKIE VIRUSES IN PARALYTIC POLIOMYELITIS. E. C. CURNEN and J. L. MELNICK, Pediatrics **8**:237 (Aug.) 1951.

Tests for the presence of Coxsackie virus were carried out with specimens of feces and swabbings of the nasopharynx from 20 children suspected of having poliomyelitis who were hospitalized in New York during the epidemic of poliomyelitis in the summer of 1949. From the feces of two girl patients with paralysis, strains of virus, which caused fatal disease in infant mice, were isolated and identified in neutralization tests with specific immune sera as Coxsackie virus, type 1. Neutralizing antibodies against the strains from each patient were present in successive specimens of serum from both patients but rose to high titer in only one. From both patients strains of poliomyelitis virus were also recovered which produced paralytic disease and lesions typical of poliomyelitis in monkeys, following injection by the intracerebral route. The latter strains were not pathogenic for infant mice. The Coxsackie and poliomyelitis viruses which were isolated from one of these patients were tested by means of cross-neutralization tests in infant mice and monkeys, respectively, and were found not to be antigenically related to each other.

When Coxsackie and poliomyelitis viruses are found together in the same patient, evaluation of the role of each agent in the pathogenesis of associated disease is difficult. Flaccid paralysis in patients from whom Coxsackie virus has been recovered may be attributable to associated poliomyelitis virus. It has not yet been shown that a Coxsackie virus alone can induce paralytic disease in man. On the basis of present knowledge it seems reasonable for the clinician and the epidemiologist to consider typical acute paralytic illnesses as poliomyelitis until convincing evidence to the contrary is made available.

FROM THE AUTHORS' SUMMARY.

EXPERIMENTAL INTRAOCULAR INFECTION OF GUINEA PIGS WITH MUMPS VIRUS. VERN S. BOLIN, JOHN A. ANDERSON, and GLEN R. LEYMASTER, Proc. Soc. Exper. Biol. & Med. **75**:166 (Oct.) 1950.

An embryo-adapted strain of mumps virus which had undergone 52 passages in embryos was given to guinea pigs by inoculation into the aqueous humor of the anterior chamber of the eyes.

Serum was collected immediately before the virus injection and again 18 days later. The authors were able to demonstrate that chick embryo-adapted mumps virus can infect the tissues of guinea pigs' eyes after intraocular inoculation. The mumps virus has been carried through seven successive passages with study of the subsequent production of complement-fixing antibodies in the serum. Doses of virus, 6 to 10 times as large a those necessary to infect the anterior chamber, caused little or no antibody formation when introduced into the plantar spaces, the peritoneal cavity, or the heart. The authors believe that the guinea pig is a suitable animal for the study of mumps-virus injections when inoculations are made in the anterior chamber of the eye.

HANSEN, Galveston, Texas.

THE RH TYPES AND THEIR CLINICAL EFFECTS IN EGYPT. SALAH EL-DEWI, J. Roy. Egyptian M. A. **34**:283 (April) 1951.

The author lists the statistical incidence of the various Rh factors in Egypt. Thirty-three per cent of the population are Rh negative, which leads to an expected incidence of erythroblastosis of 1 in 1,000 births.

McGUIGAN, Evanston, Ill.

REACTIONS TO STRAIGHTENING OF THE BODY AXIS IN THE NEWBORN. ANDRÉ-THOMAS, Presse méd. **58**:672 (June 14) 1950.

This is a detailed account, with excellent photographs, of the reaction of the newborn in response to change of position. It concerns particularly the tendency of the body to assume a position of extension (straightening reaction) when the baby is held in "vertical suspension," or when the head or the foot are forcibly extended. Examples are also given of abnormal reactions occurring when nervous-system damage is present.

DAFFINEE, Melrose, Mass.

DOES SCARLET FEVER EXIST IN THE TROPICS? EUGENE STRANSKY and NATALIA S. FELIX, Ann. pediat. **177**:15 (July) 1951.

The Dick test has been performed in a limited number of persons of all age groups in a tropical country, the Philippines. It has been found that the percentage of positive reactors is very low in infancy, while in preschool age it is almost as high as in the temperate climate. In school age children there are almost no positive reactions, and in adults definitely none any more. Since scarlet fever as a clinical entity is not observed in the tropics, scarlet fever in the Philippines is without any exception a subclinical infection. The reason for it cannot be discussed for the time being.

The authors add that they have made a larger-scale examination of susceptibility to diphtheria, by means of the Schick test. The results have been published in the Philippines. Diphtheria is relatively frequent in the tropics, although less frequent and more benign than in the temperate climate. The percentages of positive reactors in different age groups is almost analogous to those in the temperate climate.

FROM THE AUTHORS' SUMMARY.

NEURONEGETATIVE DISTURBANCES IN POLIOMYELITIS: 2. TROPHIC DISTURBANCES. H. ZELLWEGER and H. MORF, Helvet. paediat. acta **5**:434 (Nov.) 1950.

The trophic disturbances accompanying anterior poliomyelitis do not, as a rule, run parallel to the motor lesions. Trophic disturbances are attributed to change in the vasomotor nervous system. Objective evidence of these changes can be obtained by capillaroscopy, skin thermometer readings, and oscillometric measurements. Skin temperature and oscillometric response are increased during the initial phase only on the affected side, and later, during the paretic stage, both these measurements are found to be decreased on the affected side as compared with the unaffected normal side. Energetic treatment aimed at overcoming these vasomotor changes should become an essential part of poliomyelitis therapy. Cases are described to illustrate results obtained with both physical therapy and sympathectomy.

FROM THE AUTHORS' SUMMARY.

SHORT-WAVE TREATMENT OF HYPERTONY OF MUSCLES IN CASES OF POLIOMYELITIS ANTERIOR. H. B. MENKE, Schweiz. med. Wchnschr. **81**:842 (Sept. 1) 1951.

Three children have responded well to short-wave treatment of hypertonic and painful muscles due to poliomyelitis.

AMBERG, Rochester, Minn.

BRONCHOPNEUMONIA IN THE COURSE OF DIPHTHERIA. BRUNO GARAU, Ann. ital. pediat. **3**:224 (No. 3) 1950.

Having studied 28 cases of bronchopneumonia in diphtheria, in children between 2½ months and 4 years old, the author concludes that such forms, although often presenting an important congestive and hemorrhagic aspect, do not reveal histologic findings which are specific and significant. The pathogenesis of these forms is examined.

FROM THE AUTHOR'S SUMMARY.

PATHOLOGICAL ANATOMY OF THE LIVER IN DIPHTHERIA. BRUNO GARAU, Ann. ital. pediat. **3**:517 (Dec.) 1950.

The author examined pathoanatomical changes of the liver in 29 children, between 2½ months and 4 years old, with diphtheria. The microscopic picture was characterized by degenerative changes, even necrosis, diffuse congestion, and dilatation of capillaries and central veins. In 10 cases there was infiltration of lymphomonocytes, sometimes few, sometimes numerous, in the portal canals. Such infiltration often enlarges in peripheral areas of hepatic lobules. Small intralobular infiltrates were observed in three cases.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF TETANUS NEONATORUM ON THE BASIS OF 2 CASES. L. MARTONI, Clin. pediat. **33**:210 (April) 1951.

Penicillin (200,000 to 400,000 units daily), in addition to tetanus antitoxin and sedatives, was used in the treatment of two patients with tetanus neonatorum. Both infants recovered, medication being discontinued in one case on the 17th day and in the other on the 49th day. These were the only cases of the disease in the past five years at the Pediatric Clinic in Bologna, Italy.

HIGGINS, Boston.

PENICILLIN AS A CURE OF SCARLET FEVER AND ITS COMPLICATIONS. M. DE GIROLAMO, Minerva Pediat. **2**:119 (March) 1950.

One hundred and ten children with scarlet fever have been treated with penicillin at the Pediatric Clinic of the University of Genoa. Routine doses of 120,000 to 160,000 units were administered twice daily for eight days. Marked improvement was noticed from the time of the first injection. Complications were very few. The hemolytic Streptococcus usually disappeared from the throat after the first two days. The children were discharged from the hospital 10 days after the onset; no new cases appeared as a result of contacts with the discharged patients. There is a theoretical possibility that intensive treatment may prevent children from getting a lasting immunity.

HIGGINS, Boston.

HEMOGLOBIN METABOLISM IN SCARLET FEVER. P. TOLENTINO, Pediatria **58**:885 (Nov.) 1950.

Nineteen of 20 patients with scarlet fever were found to have markedly greater bilirubinemia and a higher hemolytic index during the exanthematous stage than they had about 10 days later during the convalescent stage of the disease. Hyperhemolysis, combined with some liver insufficiency and a limited bilirubin excretion, would seem to explain the subicteric appearance of patients following the exanthematous stage of scarlet fever.

HIGGINS, Boston.

BIOCHEMICAL THERAPY FOR WHOOPING COUGH. G. COCOZZA and R. FEROLA, Pediatria **59**:329 (May) 1951.

For streptomycin or chloramphenicol to be effective in the treatment of infants with whooping cough, early use of the drugs is imperative. Whooping cough vaccine was found to be of value in preventing relapses.

HIGGINS, Boston.

HEMATOLOGICAL STUDY OF WHOOPING COUGH (PERTUSSIS). EDWARDO JARDON, Acta pediat. españ. **8**:1047 (Sept.) 1950.

Jardon states that leucocytosis is a fairly constant finding in children under one year with whooping cough, but that there is neither the lymphocytosis nor the eosinophilia encountered in older children with whooping cough. Neutrophiles are slightly increased, and monocytes and basophiles slightly decreased. The sedimentation rate is diminished, or at least not increased, in the catarrhal stage in 85% of cases, which differentiates this stage from the convulsive or paroxysmal stage in which the sedimentation rate is always increased. There is a constant hypoprothrombinemia, which is the rationale for the use of vitamin K in treatment.

These findings are as pathognomonic of pertussis as the positive bacillus in a cough plate. The existence of minute cerebral hemorrhages is more persistent because of the hypoprothrombinemia. The lack of prothrombin in turn is due to hepatic stasis, which in turn is an initiative factor in the production and continuation of coughing paroxysms.

ALLEN, Santa Fe, N. M.

INCIDENCE OF MENINGOCOCCUS MENINGITIS IN THE FERNANDES FIGUEIRA INSTITUTE FROM 1940 TO 1947. JORGE BARATA and JULIO C. LOPES, J. pediat. **16**:59 (April, May, June) 1950.

Fifty-one cases of meningococcus meningitis are reported and discussed. Five per cent of the cases occurred in children in the first year of life, 22% in children between 1 and 2 years old, and 60% in children of the remaining preschool ages. Seven patients died, three of whom were transferred from another institution. Treatment was with penicillin and sulfadiazine.

CHRISTOPHERSON, Wilmette, Ill.

PERTUSSIS AND THE NERVOUS SYSTEM. BUENA VENTURA FELIP VILA, Acta pediat. españ. **8**:1169 (Oct.) 1950.

The author reviews the literature concerning nervous-system sequelae to whooping cough, and presents five cases of his own. The children reported upon are all under 2½ years old but only two were very young infants. Most of them were poorly nourished at the onset and could be said to have constitutionally poor nervous systems. Without minimizing the importance of environment, state of nutrition, and psychosomatic aspects, the author points out that many of these children plainly have brain lesions. It has been the theory that the nervous-system symptoms were due to peripheral reflex excitation of the bronchiotracheal region, but autopsies continue to show lesions of the nervous system, such as edema, hemorrhage, especially petechial, and actual degeneration of tissue.

Lumbar punctures yielded fluid compatible with a serous, lymphocytic aseptic meningitis. The cause may be toxin of the bacillus Hemophilus or a neurotropic virus associated with the causal organism. In all five cases studied the children had convulsions at the onset. Motor symptoms predominated, and in one case there was a residual spastic paralysis of one arm and hand. In two cases there was impairment of intelligence. The term postpertussis encephalopathy has been proposed for this condition.

Treatment is purely symptomatic, but vitamin K should always be used. Prophylaxis in the form of immunization, early use of antibiotics, and better nutrition may reduce these cases. The serious lesions developed between 15 and 30 days after the onset of pertussis.

ALLEN, Santa Fe, N. M.

STREPTOMYCIN IN WHOOPING COUGH. PAULO RÔXO DA MOTA, Arq. pediat. **22**:33 (July) 1950.

Forty-six children with whooping cough, all under 3 years old, were treated with streptomycin with very good results. The dosage used was 60 mg. per kilogram of body weight per day, administered intramuscularly for five to seven days.

CHRISTOPHERSON, Wilmette, Ill.

POLIOMYELITIS, EPIDEMIOLOGY IN VALPARAISO. SANTAGO MUZZO, HECTOR PUMARINO, ISRAEL ROIZBLATT, and JOSE BENGOA, Rev. chilena pediat. **22**:248 (June) 1951.

Poliomyelitis has increased a great deal in Chile in the last few years. Statistical studies in Valparaiso show a marked increase in this disease in the last five years and especially in the first half of the present year (53.8% of the total cases presented). Sixty cases have been studied during a period of five years. A mortality rate of 14% has been reported. In 10% of the above reported cases the form of the disease was bulbar or cerebral, and in all of these it was fatal. Authorities on this disease insist that an early diagnosis of this very severe form of poliomyelitis is absolutely necessary in order to begin early treatment which may save the patient's life.

FROM THE AUTHORS' SUMMARY.

CLINICAL AND EPIDEMIOLOGICAL RESULTS OF PENICILLIN TREATMENT OF SCARLET FEVER. W. HANGARTER and F. SIEBERT, Deutsche med. Wchnschr. **76**:1005 (Aug. 17) 1951.

On the basis of 127 patients treated with penicillin and 48 patients without penicillin treatment, it is stated that in the future every case of scarlet fever should be treated with penicillin.

AMBERG, Rochester, Minn.

RESULTS OF PHYSICAL TREATMENT OF POLIOMYELITIC PARALYSIS. H. JANTSCH and I. MULLER, Wien. klin. Wchnschr. **63**:385 (May 25) 1951.

The physical treatment of poliomyelitic paralyses includes constant use of galvanic and stimulating electricity, massage, and intensive therapeutic gymnastics, not limited locally.

AMBERG, Rochester, Minn.

PENICILLIN TREATMENT OF SCARLET FEVER. E. LORENZ and I. HAIDVOGL, Wien. klin. Wchnschr. **63**:460 (June 22) 1951.

The treatment of scarlet fever with penicillin is discussed on the basis of a study of 2,437 patients up to 15 years old who were observed during a three-year period. Of these, 236 patients were treated with penicillin, and 260 were not. Active immunization is regarded as useless. The antibiotic was injected in aqueous solution six times a day for six days in a daily dosage of 8,000 units per kilogram of body weight. The rapid disappearance of hemolytic streptococci from the throat is stressed, although hemolytic streptococci, which were penicillin-sensitive, recurred after a period ranging from 9 to 33 days. Strict isolation is demanded, since the number of complications in a penicillin-treated group increased when placed in a ward, surpassing even those in a group not treated with penicillin. The specific antibody formation does not seem to be injured.

AMBERG, Rochester, Minn.

NEW METHOD OF TREATMENT OF SCARLET FEVER AND ITS REASONS. L. KULIN, Wien. klin. Wchnschr. **63**:542 (July 27) 1951.

Cyclic administration of penicillin is recommended. The drug should be administered during the first 5 days of the disease, from the 9th to the 11th, the 17th to the 19th, and the 23rd to the 25th day. By this method it is assumed that the complications of the first and second disease can be obviated.

AMBERG, Rochester, Minn.

THE SCARLET FEVER PROBLEM. V. DUANCIE, Wien. klin. Wchnschr. **63**:777 (Oct. 12) 1951.

Clinical observations of more than 7,000 cases of scarlet fever over the years distinguishes three main groups. The first group, comprising about 60% of the cases, has typical scarlatinal angina and exanthema; the second group, about 25%, is characterized by typical exanthema but by angina which is atypical and not distinguishable from the usual angina; the third group, which occurs in about 15% of cases, has typical exanthema but no involvement of tonsils and throat. The sole cause of scarlet fever is seen in the hemolytic Streptococcus with its bacterial and toxic components. Without the latter, localized lesions are produced, such as those of erysipelas, furunculosis, and phlegmons. The existence of a specific scarlet fever Streptococcus

is denied. The toxin elicits the defense mechanism of the organism, thus producing antibodies leading to immunity, while this response to the Streptococcus is minimal or absent. That the skin of the face and the forehead often remains free from exanthema is attributed to local immunity. Antibodies arising in the tonsils and their vicinity are carried by the lymph vessels to the skin of the face and the forehead with the result that these regions receive more antibodies than other parts of the body.

AMBERG, Rochester, Minn.

MEASLES ENCEPHALITIS: CLINICAL AND ELECTROENCEPHALOGRAPHIC FINDINGS. E. B. HOLMGREN and E. G. JACOBSSON, Svenska läk.-tidning. **46**:637 (Feb. 24) 1949.

Since 1925, forty-eight cases of measles encephalitis have been treated at the Hospital for Epidemic Diseases in Stockholm, Sweden. Symptomatology, diagnosis, course, prognosis, and pathology are discussed. The authors stress the common occurrence of paresis of the urinary bladder during the acute stage. Twelve encephalitic cases and four uncomplicated cases of measles were studied electroencephalographically. The children in the latter cases displayed normal tracings. Of the children in the former cases, 11 had pathologic electroencephalograms, which, however, became normal rather rapidly.

WALLGREN, Stockholm, Sweden.

FIRST CONTRIBUTION TO THE STUDY OF POLIOMYELITIS IN SWEDEN. STATE BOARD OF HEALTH, Svenska läk.-tidning. **46**:1193 (June 3) 1949.

In two official reports to the Royal Medical Board in August and October, 1881, the medical officer of health in the district of Umeå in the north of Sweden has given detailed information on 18 cases of acute anterior poliomyelitis which occurred in his district from July to November of that year. These are the first known Swedish cases of the disease. The summary of the symptoms and the description of the disease correspond fairly well to present knowledge of acute anterior poliomyelitis.

WALLGREN, Stockholm, Sweden.

COXSACKIE VIRUS PRODUCING THE CLINICAL PICTURE OF NONPARALYTIC POLIOMYELITIS. SVEN GARD, Svenska läk.-tidning. **47**:285 (Feb. 10) 1950.

The author reviews the present knowledge of Coxsackie-virus infection, especially with regard to poliomyelitis, emphasizing the differential diagnostic signs: demonstration of Coxsackie virus in the stools, body fluids, or pharynx by inoculation in 2-to-3-day-old suckling mice and demonstration of antibodies during convalescence. So far eight strains of Coxsackie virus have been demonstrated in Sweden, and 30 to 50% of all examined blood serum samples contained specific antibodies. Two cases of typical Coxsackie-virus infections, with signs and symptoms of meningitis, are reported.

WALLGREN, Stockholm, Sweden.

EFFECT OF MEASLES ON THE NEPHROTIC SYNDROME. GÖSTA ÖBERG, Upsala läkaref. för H. **54**:85 (March 15) 1949.

The effect of measles on two children with albuminuria is reported. One patient, a boy of 2½ years, had a typical nephrotic syndrome which disappeared in connection with measles. The second patient, a boy of 3½ years, had albuminuria that had remained after an attack of acute nephritis. The mechanism of the therapeutic effect is discussed, and the influence of infectious disease on the plasma protein is stressed.

WALLGREN, Stockholm, Sweden.

PENICILLIN TREATMENT AND ISOLATION OF SCARLET FEVER PATIENTS. H. HAUGE, Tidsskr. norske laegefor. **70**:87 (Feb. 1) 1950.

A report is made of a study of 950 patients with scarlet fever treated with penicillin and isolation for 8 to 9 days. Of cases which were without complication at the time of admission of the patients 9.2% subsequently displayed complications.

WALLGREN, Stockholm, Sweden.

GAMMA GLOBULIN IN MEASLES PROPHYLAXIS. BJARNE JORDAL, Ugesk. læger **111**:59 (Jan. 20) 1949.

Fifteen hundred seventy children, 6 months to 12 years old, were treated with 0.5 to 5 ml. of gamma globulin prepared from pools of plasma from normal adults; and 502 children, aged 6 months to 15 years, were treated instead with 5 to 20 ml. of convalescent serum. When treatment was administered within the first six days after exposure to measles, gamma globulin produced protection in 91.3 to 93.7% and convalescent serum in 96.4 to 100%. There were no untoward local reactions with gamma-globulin injections, and no known case of inoculation hepatitis occurred.

WALLGREN, Stockholm, Sweden.

POLIOMYELITIS FOLLOWING SMALLPOX VACCINATION. A. VERJAAL, Nederl. tijdschr. geneesk. **94**:2665 (Sept. 16) 1950.

Two cases are described, one in a 10-month-old girl who had been vaccinated against smallpox two and one-half weeks before the development of poliomyelitis which caused paralysis of the left leg, the site of vaccination. The second patient, a 35-year-old man, who had been vaccinated successfully on two occasions with an interval of two months, manifested poliomyelitis two and one-half weeks after the last vaccination, both legs being paralyzed. Here also the thighs had been the site of vaccination.

Although the relationship between vaccination and poliomyelitis has not yet been definitely established, the author favors the hypothesis that the vaccination wound is the portal of entry for the poliomyelitis virus. At any rate, it seems advisable not to vaccinate during a poliomyelitis epidemic and to limit vaccination as much as possible during the months of July and August, since those are the months in which poliomyelitis occurs most frequently.

VAN CREVELD, Amsterdam, Netherlands.

SERIOUS COMPLICATIONS IN EPIDEMIC PAROTITIS, M. DE GROOT, Nederl. tijdschr. geneesk. **94**:3556 (Dec. 9) 1950.

Epidemic parotitis in a 43-year-old patient was complicated by bilateral orchitis and epididymitis which made the patient seriously ill. The complication was characterized by continual fever, bradycardia, splenomegaly, inflammation of various mucous membranes, and headache. The author also points out that in maternal infection with mumps virus there is a possibility of intrauterine injury of the fetus.

VAN CREVELD, Amsterdam, Netherlands.

USE OF BEEF RESIDUE HYDROLYSATE FOR THE PRODUCTION OF POTENT DIPHTHERIA TOXIN. CHAO-MING HUNG and KUO-PIN SUNG, Chinese M. J. **67**:271 (May) 1949.

Routine production of diphtheria toxin requires a medium containing amino acids, which are not readily obtainable in China. The authors employed a beef residue hydrolysate and added to it growth-promoting accessories, prepared according to the method of Mueller and Miller. Toxin produced with this medium was superior to one obtained with casein hydrolysate.

MACDONALD, Pittsburgh.

Diseases of Blood, Heart and Blood Vessels and Spleen

PITUITARY ADRENOCORTICOTROPIC HORMONE (ACTH) AND 11-DEHYDRO-17 HYDROXY CORTICOSTERONE (CORTISONE) THERAPY IN LEUKEMIAS AND LYMPHOMAS OF CHILDREN. C. E. SNELLING, W. L. DONOHUE, B. LASKI, and S. H. JACKSON, Pediatrics **8**:22 (July) 1951.

This report concerns the results obtained with either corticotropin (ACTH) or cortisone in the treatment of 16 children with leukemia and 1 with lymphosarcoma. For 13 patients the primary hormone treatment was with corticotropin, and for 4 patients, cortisone was used initially. Over 50% of the patients had a complete hematologic response lasting from 3 to 13 weeks. In the majority of those who received a second course the disease was either completely or partially refractory to treatment.

Biochemical studies were made on none of the patients. There was little or no correlation observed between the sodium or potassium retention and the effectiveness of the treatment, but there did appear to be a direct relationship between the increase in urinary 17-ketosteroids and successful remissions.

FROM THE AUTHORS' SUMMARY.

EFFECTS OF ACTH AND CORTISONE ON LEUKEMIA. J. SCHULMAN, J. T. LANMAN, O. E. LAXDAL, and L. E. HOLT JR., Pediatrics **8**:34 (July) 1951.

The results of treatment of 14 children with leukemia with corticotropin (ACTH) and cortisone have been presented. Complete laboratory and clinical remissions lasting 1 to 33 weeks were induced in six patients; incomplete remissions were induced in two others. No favorable responses were encountered in terminal states, monocytoid leukemia, and granulocytic leukemia differentiated beyond the blast stage. No relationship could be demonstrated between refractoriness to the hormones and to anti-folic-acid therapy; patients completely refractory to one agent have shown complete response to the other.

Although repeated remissions may be induced by hormone therapy, increasing resistance to the drugs tends to develop. While permanent benefit has not been obtained, corticotropin and cortisone constitute valuable additions to the therapy of leukemia.

FROM THE AUTHORS' SUMMARY.

THE SURGERY OF PATENT DUCTUS ARTERIOSUS. R. H. BETTS and T. THOMAS, J. Indian M. A. **20**:309 (June) 1951.

Current literature on patent ductus arteriosus is reviewed and diagnostic points outlined. The authors advise operation before cardiac decompensation or endarteritis occur.

McGUIGAN, Evanston, Ill.

TWO CASES OF COMPLETE TRANSPOSITION OF THE GREAT VESSELS. R. JACCARD, Helvet. paediat. acta **6**:225 (June) 1951.

Anatomical and clinical details are presented in two cases of complete transposition of the great vessels. Additional malformations in one case consisted of absence of the atrium and interventricular septum (cor biloculare). The pulmonary veins in this case opened into a sinus venosus which did not communicate with the heart, the blood reaching the systemic circulation by a persistent embryonic vein. The second case showed all the classic features of transposition of the large vessels, including patent foramen ovale and persistent ductus arteriosus.

GRULEE, Evanston, Ill.

TRANSFUSION REACTIONS AND INTRAVENOUS PROCAINE. E. GRASSO, Minerva pediat. **2**:210 (May) 1950.

Intravenous injection of procaine hydrochloride (5 cc. of 1% solution per 100 cc. of blood) diminished markedly post-transfusion reactions in children receiving transfusions with blood properly matched or from universal donors.

HIGGINS, Boston.

FIRST STUDIES WITH AXIAL TRANSVERSE STRATIGRAPHY, COMBINED WITH FRONTAL STRATIGRAPHY IN CASES OF PATENT DUCTUS BOTALLI. R. BULGARELLI and L. OLIVA, Minerva pediat. **3**:259 (May) 1951.

Many roentgenograms of proved cases of patent ductus arteriosus in children are shown. The authors feel that frontal body section roentgenography (stratigraphy) and axial transverse body section roentgenography are of definite help in the diagnosis of this condition.

HIGGINS, Boston.

A Case of Double Aortic Arch, Probably Associated with Roger's Disease, and 2 Proved Cases of Roger's Disease, Studied by Transverse Axial and Frontal Stratigraphy. R. Bulgarelli and L. Oliva, Minerva pediat. **3**:299 (May) 1951.

Body section roentgenography (stratigraphy), especially of the transverse axial type, is shown to be of definite diagnostic value in diagnosing double aortic arch. This procedure is also helpful in establishing a diagnosis of patent interventricular septal defect.

Higgins, Boston.

New Technique of O'Connell in Treatment of Coarctation of the Aorta. J. Pedro R. de Ledesma, Acta pediat. españ. **9**:336 (March) 1951.

The author describes various operative procedures for correction of coarctation of the aorta, and gives details of the simplified method used by O'Connell at St. Vincent's Hospital, Dublin, Ireland. Illustrations are included showing the adult type, the childhood type, and five variations of this anomaly.

Details of the operation are illustrated by drawings and carefully explained. The advantages of this procedure over others are (1) it is less dangerous as a plastic procedure than resection; (2) it is not necessary to use the subclavian artery for anastomosis, and therefore there is not the danger of poor circulation to the arm, and (3) the technique is simple. Ledesma believes that in many cases it will take the place of more difficult resection techniques.

Allen, Santa Fe, N. M.

Bone Lesions of Leukemia in the Infant. Julio Hasbun and Raul Eberhard, Rev. chilena pediat. **21**:289 (July) 1950.

The authors studied roentgenograms of the bone lesions in nine cases of lymphatic leukemia in children. They reviewed the literature and analyzed the roentgenologic picture and the differential diagnosis.

From the Authors' Summary.

Acute Lymphatic Leukemia in Children. Yung-En Kao, Tung-Hai Chao, and Chien-Wu Hu, Chinese M. J. **67**:203 (April) 1949.

In 26,383 Chinese children outpatients the authors encountered two cases of acute lymphatic leukemia. Both were in boys. In contrast, in a similar survey, 14 cases were discovered in 25,246 hospital admissions to Babies Hospital, New York.

Macdonald, Pittsburgh.

Diseases of Nose, Throat, and Ear

Congenital Auricular Fistula. Benjamin Bofenkamp, Minnesota Med. **34**:329 (April) 1951.

Congenital auricular fistula has been explained as an inclusion of epidermis in one of the grooves existing between the six tubercles forming the external ear. The condition may be bilateral or unilateral. When the tract becomes infected, it may be mistaken for sebaceous cyst. Permanent cure can be obtained by surgical removal following injection of methylene blue.

Stoesser, Minneapolis.

Effects of Limited Hearing on the Development of Speech in Children Under 3 Years of Age. H. C. Huizing and Doreen Pollack, Pediatrics **8**:53 (July) 1951.

Natural development of speech elements in acoustically handicapped children has been proved possible provided that the limited hearing is detected at a very early age by new testing procedures. It is achieved under clinical conditions by the use of individual hearing aids which provide auditory stimulation from the age of 2 years, or even earlier, upwards. Special treatment is necessary, and training of the parents plays an important part. If a listening function is not established at an early age, there is a danger that children with limited hearing will ignore sound or will actually find it annoying. Future success is dependent upon the hard-of-hearing child

being educated together with normal-speaking children, with the reservation that he will need special arrangements for speech therapy and speech reading. New specifications should be made concerning the admission of acoustically handicapped children into special schools, and the considerations mentioned above should be applied.

FROM THE AUTHORS' SUMMARY.

INCREASED FREQUENCY OF AUDITORY LESIONS ON COMBINED INTRASPINAL AND INTRAMUSCULAR ADMINISTRATION OF DIHYDROSTREPTOMYCIN. MARIANNE KAHL, Deutsche med. Wchnschr. **76**:944 (July 20) 1951.

Although the number of observations is somewhat limited, it is concluded that combined intraspinal and intramuscular administration of dihydrostreptomycin is followed as frequently by severe damage of the acoustic nerve as is that of streptomycin. It seems probable that dihydrostreptomycin is even more toxic. The observations were made on patients of the University Children's Clinic at Frankfurt, Germany.

AMBERG, Rochester, Minn.

TRACHEOTOMY IN SUBGLOTTICAL LARYNGITIS AND LARYNGOTRACHEOBRONCHITIS. WILLEM WAGEMANN, Med. Klin. **46**:841 (Aug. 3) 1951.

In two boys, 6½ and 5 years old, tracheotomy became unavoidable because of severe acute subglottical laryngitis and tracheobronchitis probably due to influenza infection. The indication for tracheotomy under such circumstances and the postoperative treatment are discussed.

AMBERG, Rochester, Minn.

Diseases of Lungs, Pleura and Mediastinum

SINOBRONCHITIS IN INFANTS AND CHILDREN. WALTER C. PRICE, J. Pediatrics **38**:590 (April) 1951.

The author has studied the association of chronic sinusitis with chronic bronchial disease. Three hundred eighty-four children were studied. The diagnostic data included history, physical examination, and roentgenograms of the sinuses and the chest. The results were as follows: 1. In a control group of children with no respiratory symptoms 7.7% had roentgenographic evidence of sinobronchitis. 2. Of children with chronic respiratory disease 37.7% had sinobronchitis. 3. Of children with sinobronchitis 46.8% were under 9 years old, and the more severely ill patients in this group were under 5 years old. The author concludes that sinusitis is frequently associated with chronic lower respiratory infection in children.

MACDONALD, Pittsburgh.

INTRALOBULAR SEQUESTRATION OF LUNG ASSOCIATED WITH AN ABNORMAL PULMONARY ARTERY. H. D'ARCY SUTHERLAND, Clin. Rep. Adelaide Child. Hosp. **2**:1 (May-Nov.) 1951.

The author describes four cases of abnormalities of lung growth associated with aberrant blood supply. He points out the need for recognizing the possibility of such aberrant blood supply and postulates that these congenital dysphasias of lung tissue are dependent upon the vascular anomalies.

MCGUIGAN, Evanston, Ill.

ALTITUDE TREATMENT IN BRONCHIAL ASTHMA IN CHILDREN. H. WISSLER, E. KONG, and C. GASSER, Helvet. paediat. acta **6**:235 (June) 1951.

Observations on 202 asthmatic children during several months' treatment in two Alpine stations, Davos (5,000 feet, 102 children) and Celerina, Engadine (6,000 feet, 100 children), are described. During the climatic treatment 87% of the children were free of attacks; all of them were in good physical condition, felt well, got stronger, and gained weight. After their return (observation period one to six years, average three years) 20% had no more attacks, 55% were very much improved, and 25% had attacks as before. On the basis of these experiences, recommendations are made as to duration of such treatment.

GRULEE, Evanston, Ill.

Diseases of Gastrointestinal Tract, Liver, and Peritoneum

THE PATHOLOGIC PHYSIOLOGY OF CONGENITAL MEGACOLON. ROBERT B. HIATT, Ann. Surg. **133**:313 (March) 1951.

Motility studies suggest that congenital megacolon is a disease in which the underlying defect is a disorganization of the peristaltic reflex in the rectum and/or lower sigmoid, and in which there is a delicate balance between obstruction and the compensatory mechanisms for overcoming that obstruction, i. e., hypertrophy and dilatation. In order to cure congenital megacolon, it is obviously necessary to remove this entire segment of lower sigmoid and rectum.

Three general groups of congenital megacolon resulting from variations in the pathologic picture are discussed. The author discusses the cause of death in congenital megacolon. Death in the newborn period is occasionally seen when obstruction causes perforation of the sigmoid before the compensatory mechanism of hypertrophy and dilatation can become established. Perforation after the newborn period is rare, but mucosal ulceration is common. The author calls attention to the role of water intoxication following tap-water enema in these cases.

BANTIN, Omaha.

THE SURGICAL TREATMENT OF CONGENITAL MEGACOLON. ROBERT B. HIATT, Ann. Surg. **133**:321 (March) 1951.

The principle of total removal of the nonpropulsive segment of the rectum and the sigmoid for cure of congenital megacolon is discussed. Three cases are presented in detail to illustrate the three types of congenital megacolon.

BANTIN, Omaha.

THE PROBLEM OF ESOPHAGEAL REPLACEMENT BY JEJUNUM WITH PARTICULAR REFERENCE TO INFLUENCE UPON CIRCULATION OF STAGING THE DIVISION OF MESENTERIC VESSELS. HARRIS B. SHUMACKER JR and J. STANLEY BATTERSBY, Ann. Surg. **133**:463 (April) 1951.

Esophageal replacement has been accomplished successfully by utilizing the stomach, the jejunum, and tubes of skin. The use of tubes of skin has proved a rather tedious procedure. The use of the stomach has proved generally very satisfactory, but there are some potential disadvantages in using the stomach for such a purpose. The use of jejunum has certain obvious advantages. It is almost precisely the proper size, and it and the esophagus both normally have alkaline secretions.

The authors report their experiments with rats and dogs. One case in a human is reported of successful antethoracic jejunal transplantation for by-passing a strictured esophagus, utilizing this principle.

BANTIN, Omaha.

SURGICAL EMERGENCY OF DIAPHRAGMATIC HERNIA IN INFANCY. CONRAD J. BAUMGARTNER and ROBERT F. SCOTT, Arch. Surg. **61**:170 (July) 1950.

Recognizing the fact that many infants born with congenital hernia die in the first few hours or days of life, owing to respiratory and cardiac embarrassment before surgical intervention can be instituted, the authors were prompted to review the cases of congenital diaphragmatic hernia occurring during the first year of life at the Los Angeles County Hospital (Medical Unit) between 1929 and 1949. Only infants who were less than one year old, of whom there were 13, were selected. Six were not operated upon, and seven were operated upon.

All infants not operated upon died within three days. In only one case was the correct diagnosis suspected, but in all cases the diagnosis was confirmed at postmortem examinations. Among the seven infants operated upon, three recovered. The first four infants were operated upon by the thoracic route, with a resulting high mortality. The authors conclude that with proper administration of oxygen, fluids, and blood, and with positive pressure anesthesia and an abdominal subcostal approach, a relatively low mortality should be expected.

KAISER, Rochester, N. Y.

AUREOMYCIN IN THE TREATMENT OF FIBROCYSTIC DISEASE OF THE PANCREAS. D. STOWENS, Pediatrics **8**:60 (July) 1951.

A group of patients with fibrocystic disease of the pancreas were treated with aureomycin over periods of 12 to 24 months. Gratifying clinical improvement and increases in utilization of dietary protein were observed.

FROM THE AUTHOR'S SUMMARY.

OBSERVATIONS ON THE CYSTIC STAGE OF E. HISTOLYTICA IN ABSCESSES OF THE HUMAN BOWEL. RYLE A. RADKE, Proc. Soc. Exper. Biol. & Med. **76**:831 (April) 1951.

After careful cleansing of the fecal stream overlying amebic abscesses, material containing cysts of Endamoeba histolytica was aspirated from the abscesses in the bowel wall of 25 patients with intestinal amebiasis. The findings of the author suggest that cysts of E. histolytica may be formed within the tissues rather than in the fecal stream.

HANSEN, Galveston, Texas.

CONGENITAL MEGACOLON ASSOCIATED WITH DEFECT OF INTERVENTRICULAR SEPTUM. B. DEMIRAG, Ann. pædiat. **177**:187 (Sept.) 1951.

A case of congenital megacolon associated with a defect of the intraventricular septum of a 4-month-old baby is reported. The literature on etiological factors of congenital megacolon is reviewed.

FROM THE AUTHOR'S SUMMARY.

HISTOPATHOLOGICAL ASPECTS OF THE DUODENUM IN HYPERTROPHIC ANTROPYLORIC STENOSIS OF INFANTS. G. NIERO, Clin. pediat. **32**:119 (March) 1950.

On the basis of five cases, it was noted that the first portion of the duodenum is much thicker in infants with pyloric stenosis than in normal infants. This hypertrophied musculature of the duodenum appears to be due to an altered formation and function of Auerbach's plexus, which thus seems to play a major role in the genesis of the condition.

HIGGINS, Boston.

CHRONIC INTUSSUSCEPTION WITH ATYPICAL COURSE, DIAGNOSED AT OPERATION. V. SULAS, Minerva pediat. **3**:449 (Aug.) 1951.

In an 11-year-old girl an intestinal obstruction gradually developed. The preoperative diagnosis was obstruction due to adhesions from an appendiceal abscess. Upon operation, an ileocolic intussusception was found; a hemicolectomy and a lateral-lateral anastomosis of the ileum and the transverse colon were performed. The patient had a satisfactory convalescence, and the anastomosis has continued to function well.

HIGGINS, Boston.

ANTIBIOTIC TREATMENT OF ACUTE APPENDICITIS IN CHILDREN. ANTONIO RIGHINI, Riv. clin. pediat. **48**:759 (Dec.) 1950.

Some observations on the present therapy of acute appendicitis are made. The author describes and compares the results in a series of 155 patients treated with operation as well as with parenteral and endoperitoneal administration of sulfonamides, penicillin, and penicillin streptomycin.

FROM THE AUTHOR'S SUMMARY.

CYSTIC FIBROSIS OF THE PANCREAS. OSCAR CORREA B., ALFREDO DEL RIO, ALFREDO VARGAS, and RAUL MOLINA, Rev. chilena pediat. **22**:253 (June) 1951.

Two new cases of pancreatic fibrosis seen at the Luis Calvo Mackenna Children's Hospital are presented. These two, with another recently published, are the first three cases of this entity found in the above-mentioned hospital since July, 1942 (the date of its foundation), a period during which 19,492 patients have been hospitalized and 1,794 autopsies carried out.

The first case was that of a newborn infant admitted on the third day of life with a history of lack of passage of meconium, vomiting, and pronounced abdominal distention. Upon operation a marked dilation of the small bowel, especially of the last portion of ileum, was found, which appeared full of blackish, inspissated, putty-like meconium. The infant died two days later, and

at autopsy bronchopneumonia and severe lesions of the pancreas, characterized by marked perilobular and intralobular fibrosis, dilation of the acini and ducts, and cysts, were encountered.

The second patient was an atrophic infant, approximately 7 weeks old, hospitalized due to a severe acute nutritional disturbance. When she recovered from this condition, she failed to gain in weight, and afterwards septicemia developed which was resistent to antibiotics. Postmortem examination revealed bronchopneumonia and pronounced fibrosis of the pancreas, the lobular structure of which appeared markedly altered due to invasion of conjunctive tissue into the interior of the lobules.

FROM THE AUTHORS' SUMMARY.

Nervous Diseases

BENIGN ESSENTIAL (HEREDOFAMILIAL) TREMOR. C. H. DAVIS and E. C. KUNKLE, A. M. A. Arch. Int. Med. **87**:808 (June) 1951.

Since little attention has been given this relatively common disorder, the present report was submitted as a survey of 14 cases encountered in the outpatient or inpatient service of a general hospital during a 10-year period. The genetic history of the disorder was explored, and a limited appraisal of the value of drug and other therapy was made.

The disease is relatively benign and heredofamilial. The tremor is more or less rhythmical, either fine or coarse, with a rate of 4 to 12 per second. It is occasionally present at rest and inhibited by action, but it is generally decreased or absent at rest and present on voluntary increase in muscle tonus, as when the limb is held in a definite position (static tremor) and is in active movement (kinetic, or intention tremor). It may be accentuated on approaching a goal in point-to-point movement (terminal tremor). The tremor is aggravated by emotional tension, fatigue, or the discomfort of cold. It may be increased by the use of coffee, tea, tobacco, or alcohol in excess. It is relieved by repose, sedation, or sleep. Involvement is principally of the hands, forearms, neck, head, and face, although the tongue, larynx, diaphragm, lower extremities or, rarely, the trunk may be included. Except for the increased terminal intention tremor which may interfere with self-feeding and writing, accuracy and coordination are little involved. The characteristic negative features are the lack of increased tone and resistance to passive strength of Parkinsonism (rigidity, postural flexion, masked facies) and the presence of normal, rapid, rhythmical, alternating movements and automatic associated movements. There are no defects in reflex responses or in sensation.

Representative genetic studies demonstrate considerable variety in the patterns of inheritance. Davis and Kunkle confirm the characteristic resistance of the tremor to medicinal therapy. The proper management is explanation and reassurance. The patient must learn to live with his disability, supported by the knowledge that he will not be incapacitated. Recognition of this syndrome is important, for the tremor can be, and often is, confused with that of far less benign syndromes, such as Parkinsonism.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

SPINAL (LUMBOSACRAL) EPIDERMOID TUMOR, PILONIDAL SINUS, AND PERSISTENT MENINGITIS. E. G. FORGRAVE and K. H. ABBOTT, Bull. Los Angeles Neurol. Soc. **16**:244 (June) 1951.

The congenital defect of the midline structures of the back known as pilonidal cyst, or sinus, is so common that there may be a tendency to lose sight of the not too rarely associated congenital neoplasms of the central nervous system—epidermoid, dermoid, teratoid, and teratomatous tumors.

Forgrave and Abbott describe a case of intraspinal epidermoid (in the cauda equina) associated with a pilonidal sinus in a boy aged 2½ years. Of particular interest in this case was a complicating concurrent purulent leptomeningitis, undoubtedly resulting secondarily from residual organisms in the epidural lumbosacral area, following removal of the pilonidal cyst. After the cerebrospinal fluid became sterile, virulent organisms remained in the epidermoid tumor and in the epidural abscess. So-called plaque disease about the spinal cord above the tumor was demonstrated myelographically and surgically.

That leptomeningitis may occur several months after the removal of pilonidal sinus, as in this case, has not been observed previously. From observation in this case it would seem that infection may lie dormant for months in the spinal epidural fat and/or in the intraspinal tumor following surgical intervention upon the overlying pilonidal defect, only to result subsequently in infection of the leptomeninges, thus causing a most persistent leptomeningitis. In view of the sterile cultures obtained from the cerebrospinal fluid and the meningeal (purulent) "plaques," it would appear that the failure of the antibiotics to sterilize the tumor and the epidural abscess (positive cultures were obtained from both at the time of operation) may well have been due to the avascular nature of both the tumor and the abscess.

Finally, the authors call attention to the need to recognize the possibility of the occurrence of an intraspinal tumor in children when a pilonidal defect is evident.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

BEHAVIOR DISTURBANCES IN EPILEPTIC CHILDREN. C. BRADLEY, J. A. M. A. **146**:436 (June 2) 1951.

Bradley reports his observations on behavior difficulties in intelligent and physically intact children subject to convulsive seizures. These behavior disorders are of two general sorts. There are often behavior symptoms which are the primary, direct result of the neurophysiologic disturbances that may be recorded electroencephalographically, and that are also presumably directly related to the seizures themselves. These behavior symptoms consist of five component features: (1) erratic variability in mood or behavior, (2) hypermotility, (3) irritability, (4) short and vacillating attention span, and (5) a rather selective difficulty in mathematics as a school subject. Bradley states that such behavior symptoms are best treated medically, the most effectual preparations at present available for this purpose being the amphetamines.

Other behavior disturbances, representing the child's reaction to being ill and to the way he is handled by those about him, being subject to more variables than the primary symptoms, do not fall into any such characteristic pattern; these are less specific in nature and must be treated at the psychologic level. Thus, adequate medical management of the epileptic child involves consideration of his behavior and emotional reactions, in addition to therapy designed to control his seizures.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

HEREDITY OF EPILEPSY AS TOLD BY RELATIVES AND TWINS. W. G. LENNOX, J. A. M. A. **146**:528 (June 9) 1951.

In a study of the 20,000 near relatives of 4,231 epileptic patients, a history of seizure was obtained in 3.2%. The incidence was 3.6% if evidence of brain damage prior to the patient's first seizure was lacking, and 1.8% if such evidence was present. These percentages are, respectively, 7 and 3.5 times the incidence of epilepsy among draftees of the United States Army. As additional evidence of a genetic factor, in the group with undamaged brain (essential epilepsy) the incidence of epilepsy among relatives decreased progressively with a later onset of seizures (7.6% if onset was in infancy; 1.5% if it was after the age of 30). Corresponding incidences for the group with brain damage (symptomatic epilepsy) were 2.9 and 1.3%.

The relative influences of heredity, brain damage, and chronicity of seizures were studied in a group of 122 twin pairs affected with seizures. In twin pairs without prior brain damage, both co-twins were epileptic in 84% of the one-egg twins and in 10% of the two-egg twins. In pairs with brain damage, the corresponding incidences were 17 and 8%. In one-egg twins, concordance was usual not only with respect to seizures but also with respect to the type of seizures and to the electroencephalographic pattern. Intelligence quotients were determined for 87 twin pairs. The person's mental endowment was of most importance in the maintenance of a good intelligence. Acquired brain damage was a severe depressant; the reported bad effect of repeated seizures was not in evidence.

The genetic factor in epilepsy is probably no greater than it is in many other common diseases. The epileptic is unfairly pillorized in public opinion and in law. Assets that are transmissible,

such as sound vital organs, good intelligence, personality, and social responsibility, may outweigh the liability of a tendency to seizures. Hence Lennox feels that advice regarding marriage and children must be individualized.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

PHENACEMIDE IN TREATMENT OF EPILEPSY. M. W. TYLER, and E. Q. KING, J. A. M. A. **147**:17 (Sept. 1) 1951.

The purpose of this paper is to classify and tabulate the extensive clinical reports on the use of phenacemide (phenurone®) in the treatment of epileptic seizures, in order to attain a clearer picture of the uses and limitations of the drug.

In a series of 1,539 patients, approximately 65% showed improvement when phenacemide was given alone or in combination with other anticonvulsants, such as phenobarbital, diphenylhydantoin (dilantin®), and mesantoin® (methylphenylethyl hydantoin). In 539, or 35% of the total, the seizures were completely controlled or reduced 75% or more in frequency. In 35% of the cases phenacemide therapy was recorded as a failure, either because the treatment did not bring about improvement in the patient's condition or because it became necessary to discontinue the drug when side-effects occurred.

The side-effects most frequently seen were favorable or unfavorable personality changes. Personality changes occurred in approximately 17% of all cases and usually appeared within the first four to six weeks of the therapy. The more serious side-effects encountered were evidence of hepatic damage and changes produced on the hemopoietic system. In addition, in the order of decreasing frequency, gastrointestinal symptoms, rash, drowsiness, headache, and insomnia were produced. Four deaths due to hepatitis and two deaths due to aplastic anemia were reported prior to the initiation of controls for observing the patients.

The dose of phenacemide must be individualized on the basis of the response of the patient. It has been observed by some investigators that side-effects are less likely to develop if the dose is gradually built up to that which will control the seizures. It is recommended that if some degree of control of seizures has been obtained with other medication, such medication be continued and phenacemide added at a dosage of 0.5 gm. three times a day. The dose of phenacemide should be gradually increased above this intial one until seizures are controlled or limiting side-effects develop. An average dose of 2 to 3 gm. a day has been adequate for most adults.

Tyler and King found that phenacemide (phenurone®) has proved to be effective in controlling or definitely reducing the frequency of seizures in a fairly large percentage of patients who have not responded to other anticonvulsant drugs. The patient or his family should be fully aware of the nature of the drug and of the side-effects which may be produced. They should realize there is a certain risk, which must be weighed against the possible benefits derived from its use. The physician should instruct the patient to watch for signs of toxicity and report them promptly. Only enough phenacemide to last for a short, designated interval should be prescribed.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

TORULA [CRYPTOCOCCUS] GRANULOMA OF THE CERVICAL SPINAL CORD. A. LEY; R. JACAS, and C. OLIVERAS, J. Neurosurg. **8**:327 (May) 1951.

Infection of the nervous system with Cryptococcus histolyticus usually produces rather widespread meningoencephalitis, with a severe granulomatous reaction in the leptomeninx. Sometimes the lesions may be more limited and localized in the brain, giving rise to minute cysts, with little or no alteration of the leptomeninx. These lesions can simulate a brain tumor.

Cryptococcic granuloma limited to the spinal cord has been recorded only once prior to this report. An extensive granuloma of the cervical portion of the spinal cord in a child 8 years old is reported. The symptoms were those of compression of the spinal cord. The granuloma was removed surgically, and the child, who had severe quadriparesis before the operation, recovered completely. Study of the surgical specimen indicated that the causative organism was C. histolyticus. The authors stress the rarity of the case and advocate surgical extirpation of the granuloma in all similar cases.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

INTRACRANIAL CALCIFICATION FOLLOWING PNEUMOCOCCIC MENINGITIS. ABRAHAM LEVINSON and HANS HARTENSTEIN, J. Pediat. **38**:624 (May) 1951.

In a 2-month-old girl pneumococcic meningitis developed. She recovered, but generalized rigidity developed within a few months. Within seven months of the onset of the meningitis she still showed evidence of generalized rigidity; she had had convulsions, and she had evidence of mental retardation. Skull roentgenograms now showed scattered intracranial calcifications. Cerebral arteriography showed thrombosis of the middle cerebral artery, a possible factor in the development of calcification. However, the pathogenesis of this rare complication, intracranial calcification, cannot be definitely established in this case.

MACDONALD, Pittsburgh.

CLINICAL ASPECTS OF CEREBRAL ANOXIA IN MAN. A. T. STEEGMAN, Neurology **1**:261 (July-Aug.) 1951.

The cerebral cortex cannot withstand complete oxygen deprivation for much more than five minutes without undergoing irreversible degenerative changes. The corpus striatum in man is almost equally vulnerable, but the midbrain and medulla are more resistant. The fact that the respiratory and circulatory regulating centers in the medulla can resist anoxia longer permits survival for a variable period after the cortex is damaged irreparably. Variation in the type of symptoms reflects the degree and distribution of cerebral dysfunction, but the actual degree of pathologic damage depends on the severity of anoxia, its duration, and the method by which it is produced.

Steegman reviews the principal courses of anoxia in man and the physiologic effects of oxygen deprivation. He describes the symptoms resulting from complete cerebral anemia, partial cerebral anoxia, and anoxic encephalopathy.

On the basis of the symptoms, he suggests the following classification of anoxic encephalopathy in the residual stage:

I. Primary cortical defects
  1. Diffuse
    (*a*) Emotional instability
    (*b*) Psychotic behavior
    (*c*) Dementia
  2. Focal
    (*a*) Visual defects (central blindness, scotomata, etc.)
    (*b*) Cerebral diplegia
      Symmetrical or asymmetrical, with or without minor sensory changes
    (*c*) Speech defects (dysarthria, aphasia)
    (*d*) Frontal ataxia or tremor

II. Primarily extrapyramidal motor defects
  1. Paleostriatal
    (*a*) Parkinson-like syndrome
    (*b*) Bradykinesia without tremor
  2. Neostriatal
    (*a*) Athetosis
    (*b*) Choreoathetosis

III. Mixed forms
  Variable combinations of I and II.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

HEMOPHILUS INFLUENZAE MENINGITIS: OBSERVATIONS ON THE TREATMENT OF 110 CASES. WILLIAM G. CROOK, B. REED CLANTON, and HORACE L. HODES, Pediatrics **4**:643 (Nov.) 1949.

The results obtained in the treatment of 110 infants and children infected with Hemophilus influenzae are presented, and the various agents used in the therapy of the disease are evaluated. Eighty-seven (79%) survived; sixty-eight (62%) recovered completely. Eight of the twenty-three deaths occurred within the first 24 hours after hospital admission. Slightly over one-half the children were less than one year old. Only 69% of this group survived, as compared with 90% in the group over one year old; only 50% of the younger group recovered completely, as compared with 75% of the older group.

The plan of therapy underwent various modifications and additions during the eight year period covered in this study. Forty-four per cent of the patients were treated with specific H. influenzae rabbit antiserum and sulfadiazine; forty-eight per cent were treated with these agents together with streptomycin (and in many instances penicillin). The remaining 8% were treated with streptomycin alone or in combination with sulfadiazine. The survival and complete recovery rates of those treated with serum, sulfadiazine, and streptomycin were not significantly different from the rates of those treated with serum and sulfadiazine alone. The number of patients treated with streptomycin without serum was too few for analysis.

Specific antiserum used early and in large doses seemed to be a valuable therapeutic agent in these studies. It is believed that this antiserum should be used in the treatment of all patients, except perhaps older children who are only mildly ill.

The high cost of this serum, however, remains a major problem. Streptomycin undoubtedly is a valuable therapeutic agent in the disease; in this study, however, there has been no striking improvement in the over-all results since its introduction.

Sulfonamides and especially sulfadiazine appear to have been of limited but definite value in the treatment of this disease and their continued use in all patients is recommended. Penicillin when given in high dosages would also seem to be a helpful therapeutic adjunct when used along with other agents.

Follow-up data on 64 of the 87 surviving patients are presented.

FROM THE AUTHORS' SUMMARY.

USE OF PHENURONE® [PHENACEMIDE] FOR CONVULSIVE DISORDERS OF CHILDREN. H. M. KEITH, Proc. Staff Meet., Mayo Clin. **25**:594 (Oct. 11) 1950.

Thirty-five children were treated with phenacemide (phenurone®) for periods varying from 3 to 20 months. Keith's results show that of the 35 patients observed for three months or more, 8 (23%) are considered well and have not had any known attacks, 15 (43%) have improved, and 12 (34%) have not benefited from treatment with the drug.

These observations confirm the reports of other workers that phenacemide is a useful addition to the therapeutic agents for epilepsy. It may successfully control attacks of some patients whose attacks have not ben controlled by other forms of treatment, even though a gross neurologic defect may be present. In common with most drugs, it may produce unfavorable side-reactions, such as dermatitis medicamentosa, unfavorable personality disturbances, and, in rare cases, disturbance of hepatic function.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

HAEMANGIOMAS INVOLVING THE SPINAL EPIDURAL SPACE. A. N. GUTHKELCH, J. Neurol., Neurosurg. & Psychiat. **11**:199 (Aug.) 1948.

Guthkelch surveyed the literature relating to hemangiomas of the spinal epidural space, including those which arise from the vertebrae, and reports eight cases of his own. There are altogether 17 recorded instances of mature epidural hemangiomas and 14 cases of immature hemangioendotheliomas and hemangioblastomas. Vertebral hemangiomas, on the other hand, are usually of the mature type. They are not infrequently associated with epidural hemangiomas. Epidural tumors usually occur in the thoracic region of the spine.

Anatomically and clinically, no sharp division should be made between epidural and vertebral hemangiomas. Both are probably congenital anomalies capable of growth, the difference in type of growth depending on the activity of the surrounding tissues. Intermediate stages often occur. Both types cause compression of the spinal cord, and the clinical signs are those of progressive paraplegia with inconstant sensory changes. In a few cases, remittent attacks of paraplegia occurring during pregnancy with remission post partum were found to be caused by intraspinal hemangioma, the symptoms being precipitated by the general venous engorgement of pregnancy.

Therapeutically, however, the two types of tumor present different problems. In the case of epidural tumors, exploratory operation is necessary to establish the diagnosis; the operative

results vary with the histologic structure, and the value of x-ray therapy is questionable. In the case of vertebral hemangiomas, on the other hand, the diagnosis can be made roentgenographically, and the results of x-ray therapy are generally much better than those of surgery.

MALAMUD, San Francisco [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

SUBACUTE NECROTIZING ENCEPHALOMYELOPATHY IN AN INFANT. D. LEIGH, J. NEUROL., Neurosurg. & Psychiat. **14**:216 (Aug.) 1951.

Leigh reports the case of a boy aged 7 months who died within six weeks of a disorder of the central nervous system characterized by somnolence, blindness, deafness, and spasticity of the limbs.

The neuropathologic picture consisted in focal, bilaterally symmetrical, subacute necrotic lesions or softenings extending from the thalamus to the pons, the inferior olivary nuclei, and the posterior columns of the spinal cord. Histologically, the affected areas showed an intense vascular, microglial, and histiocytic proliferation and a less pronounced astrocytic increase. There was severe neuronal damage in these areas.

In discussing the etiology and pathogenesis, Leigh suggests that an unknown toxin or virus was responsible for these lesions or, more probably, that these lesions represent the reaction of an immature brain to the same type of nutritional deficiency which produces the Wernicke syndrome in the adult.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

ABDOMINAL EPILEPSY. M. T. MOORE, Schweiz. med. Wchnschr. **80**:1352 (Dec. 23) 1950.

Paroxysms of abdominal pain may be the only or the dominant feature associated with peculiar feelings, with nausea, pallor, sweating, occasionally vomiting, rarely diarrhea, etc. These attacks may be a symptom of epilepsy. Among cases described in detail are those of two boys, aged 11 and 12 years, both of whom had abdominal crises for a period of four to six years. In one case a severe cranial trauma preceded the attacks. In the other an allergy to various foods existed, but an antiallergic regimen did not improve matters. Anticonvulsive treatment was successful in both cases.

AMBERG, Rochester, Minn.

SMALL "AUTOMATON" OF 3 YEARS: UNUSUAL STEREOTYPY; SEQUELA OF ENCEPHALITIS. M. SCHACHTER, Lattante **22**:293 (May) 1951.

A 3-year-old girl had had encephalitis at the age of one year. She did not utter any sounds and maintained a rigid posture, with steretoyped movements of the arms and eyes; she presented the picture of an automaton. The signs are probably due to injury of the frontal lobes.

HIGGINS, Boston.

IMPORTANCE OF MATERNAL ISOIMMUNIZATION AS AN ETIOLOGIC AND PATHOGENIC FACTOR IN SOME ENCEPHALOPATHIES OF CHILDREN. G. MURANO, Minerva pediat. **2**:101 (March) 1950.

The discovery that the cells of the nervous system contain an Rh factor strengthens the hypothesis of an allergic antigen-antibody reaction in the brains of newborn infants, when there has been a maternal isoimmunization. It is certain that any brain injury in cases of kernicterus is not vascular.

HIGGINS, Boston.

TREATMENT OF PURULENT MENINGITIS WITH OCCLUSION OF THE SPINAL CANAL IN INFANTS. C. AGUILO and J. MENEGHELLO, Rev. chilena pediat. **21**:486 (Nov.) 1950.

Of 23 infants with purulent meningitis of different origin, 4 died during the first 30 hours after admission to the hospital, thus giving an over-all mortality of 17.3%. Nineteen infants were treated with a sulfonamide preparation and penicillin and/or streptomycin without resource to the intrathecal route. All patients recovered. Two infants presented a transient hydrocephalus during the acute stage of the disease, and one had a slight right hemiparesis. Two infants

sustained severe neurological damage and died afterwards, owing to intercurrent infections. One sustained a communicating hydrocephalus. Two newborn infants with meningitis due to enteric organisms recovered.

The authors conclude that intrathecal administration of either streptomycin or penicillin is unnecessary in the treatment of purulent nonmeningococcic meningitis in infancy. The dosage of the antibiotics and sulfonamides must be high, and the following dosages are recommended: penicillin, 100,000 units per kilogram in 24 hours; streptomycin, 100 mg. per kilogram in 24 hours; sulfonamides, 0.30 to 0.50 gm. per kilogram in 24 hours. The combined treatment must be continued for an average of 10 days after clinical cure and categorical improvement of the cerebrospinal fluid.

FROM THE AUTHORS' SUMMARY.

PYOCYANIC MENINGITIS. A. FAZEKAS and I. NIKODEMUSZ, Wien. klin. Wchnschr. **62**:903 (Dec. 1) 1950.

A 2½-year-old boy became sick with a purulent meningitis which proved refractory to penicillin therapy. Pyocyanic bacilli were identified in the spinal puncture fluid. Treatment with streptomycin proved successful.

AMBERG, Rochester, Minn.

CEREBRAL PERIARTERITIS NODOSA IN A 5-YEAR-OLD GIRL. J. VANEK, Pediat. listy **6**:335 (No. 3) 1950.

In a girl aged 5½ years, who had been ill for two and one-half months with encephalitic symptoms, severe vascular changes were disclosed in the brain at autopsy. Upon microscopic examination these changes appeared to be due to periarteritis nodosa involving mainly the middle and anterior cerebral artery. All other organs were found to be free of arteritic changes upon routine examination. Both the history and the clinical course failed to give a clue as to cause of the disease.

FROM THE AUTHOR'S SUMMARY.

WILSON'S DISEASE. A. K. A. GIJSBERTI HODENPIJL, Maandschr. kindergeneesk. **18**:415 (No. 11) 1950.

A family of 10 children is described in which 4 had Wilson's disease (hepatolenticular degeneration). Two of them died last year; the other two are still living and in a satisfactory condition. The remaining six children are free of symptoms.

FROM THE AUTHOR'S SUMMARY.

Psychology and Psychiatry

PROPER USE OF ANTIBIOTICS IN TREATMENT OF ACUTE OTITIS MEDIA. MIRIAM H. RUTHERFORD, California Med. **75**:98 (Aug.) 1951.

The problem of preventing loss of hearing following acute otitis media has been made more complex by the use of penicillin and other antibiotic agents which may apparently cure yet leave dangerous residual disease. The causes of loss of hearing must be recognized early if remedial treatment is to be effective. In children particularly, loss of hearing may go unnoticed for some time. Physicians who treat otitis media should feel the responsibility not only for bringing an acutely ill child back to health but also for preserving the function of the hearing mechanism. Careful examination of the ear after apparent subsidence of infection is mandatory. It is of the utmost importance to be able to recognize the tympanum in its normal state and its various pathological states and to be alert to the early signs of changes associated with loss of hearing.

PRYOR, Redwood City, Calif.

SOME VIEWPOINTS ON CHILD PSYCHIATRY. FORREST N. ANDERSON, California Med. **75**:213 (Sept.) 1951.

The author seriously questions the great tendency in recent years to seek psychiatric answers to almost all kinds of child problems. The average child has splendid capacities to solve his own growth problems, within the limits of home, school, and neighborhood. Evidence indicates

that the average parent who seeks counsel has done a rather respectable job, that in his fear of setting limits because of "how the child will feel" there is more of psychological threat to the child than in daring to move ahead comfortably and make some mistakes.

Psychiatric treatment of a child implies that the child is unable to meet situations as adequately as other children. Such treatment should be reserved, in the main, for use in situations in which the psychiatrist and the parents are willing to underwrite the implications of treatment. Treatment aimed at the vague goal of making the child "happier" is dubious. Treatment by a psychiatrist is presumably medical treatment and carries with it the advantages and disadvantages inherent in this fact. When given without carefully defining the reasons for it and the goals at which it is aimed, within medical framework, it is potentially an undesirable procedure.

PRYOR, Redwood City, Calif.

MONGOLISM IN ONE OF TWINS. G. POSTERARO, Lattante **22**:297 (May) 1951.

Twins were born 11 years after the second of two previous pregnancies. The boy was a mongolian, and the girl was normal. At the age of 14 months, the height and the circumference, respectively, of the head were 5 cm. and 4 cm. less in the boy than in the girl. Roentgenograms of the boy's skull suggested some increase in intracranial pressure. In a consideration of possible etiological factors, the author reports that the father had been intimate with a syphilitic before and during the pregnancy, and that the mother had had nausea, vomiting, headaches, tics, and epileptoid seizures and had taken large doses of quinine and ovarian extracts during the pregnancy. The Wassermann reactions of the parents and of the girl were negative, and that of the boy was questionably positive.

HIGGINS, Boston.

NEUROTIC STAMMERING, A SYMPTOM OF LATENT AGGRESSIVENESS. M. SCHACHTER, Riv. clin. pediat. **49**:461 (July) 1951.

A clinical psychological study of a girl, 13 years and 9 months old, who had already reached puberty is presented. She was affected by a form of stammering of which the intensity was more evident when she was in her mother's company than when she was at school or with other people. The clinical and psychological examination, with the help of Rorschach and Murray tests, showed that the basis of this essentially neurotic stammering was a remarkably violent aggressive impulse against a hyperanxious, restless mother who was hindering the girl's affective effusiveness somehow. The fact that the girl was an only child is duly stressed. The results obtained with the Rorschach test on the girl are compared with results already achieved through a similar study on 20 children affected by various forms of dysarthria.

FROM THE AUTHOR'S SUMMARY.

INFLUENCE OF STATE OF HEALTH AND NUTRITION ON MENTAL CAPACITY: SOCIAL HYGIENE STUDY OF GERMAN SCHOOL POPULATION. HELMUT TRAEBERT, Med. Klin. **45**:881 (July 21) 1950.

After repeated preliminary tests, data were collected on the same day, in rural districts and in small towns. Teachers estimated mental capacity, and nurses from the department of health estimated the state of nutrition of 19,000 subjects. It was evident that unfavorable nutritional conditions diminished mental capacity, though not always and not much; with poor nutritional conditions good performances became less and poor performances more frequent. The general living conditions of 30% of the subjects were classified as very bad.

AMBERG, Rochester, Minn.

INDICATION FOR TRANSORBITAL LEUCOTOMY. PETER DAL BIANCO, Wien. klin. Wchnschr. **61**:773 (Nov. 4) 1949.

A transorbital leucotomy was performed in three children under 15 years old, a 3-year-old boy, an 8-year-old boy, and a 6-year-old girl. The children were designated as having the form of imbecility known as cretinism. They became socialized and responded to educational measures surprisingly well.

AMBERG, Rochester, Minn.

Diseases of Genitourinary Tract

OVARIAN DERMOID PERFORATING THE RECTUM IN A CHILD: EXCISION BY ABDOMINO-PERINEAL PROCTOSIGMOIDECTOMY. HARRY S. BACON and S. W. EISENBERG, Ann. Surg. **133**:408 (March) 1951.

Dermoid cysts of the ovary are fairly common tumors, and, although most of them are detected during the child-bearing period, a comparatively large number are found in children. The authors report an unusual case of perforation of the rectum by an outgrowth from a dermoid cyst of the right ovary, resulting in a polypoid tumor of the rectum. The child was 7 years old. Sixteen months following operation the child was in school and leading a normal life.

BANTIN, Omaha.

OUTBREAK OF ACUTE NEPHRITIS IN ADOLESCENT SCHOOL BOYS. C. HENRY KEMPE, RICHARD W. OLMSTED, and EDWARD C. CURNEN, Pediatrics **8**:393 (Sept.) 1951.

An outbreak of acute nephritis is reported, occurring among adolescent boys who were students at a private day school. Four boys in one class had clinically typical acute glomerular nephritis. Seventeen other members of this and one other class were found to have hematuria with or without associated albuminuria. The total incidence of hematuria among the 73 students in these two classes was 29%. Fifteen of the 21 boys with hematuria still had abnormally elevated Addis sediment counts approximately seven weeks after the initial examination.

Cultures of the nasopharynx were made from 85 students. Hemolytic streptococci were detected in 11 (13%) of the boys, including 3 with hematuria. The results of attempts to identify the streptococci by serologic technics indicated that at least five immunologically different varieties were represented. Determinations of antihyaluronidase, antistreptolysin "O," and antistreptokinase in serum from 17 boys with hematuria and 20 without apparent hematuria revealed wide variations in titer but no significant difference between the two groups.

FROM THE AUTHORS' SUMMARY.

THE TESTIS: V. USE OF TESTICULAR BIOPSIES IN THE DIFFERENTIAL DIAGNOSIS OF PRECOCIOUS PUBERTY. EDNA H. SOBEL, RONALD C. SNIFFEN, and NATHAN B. TALBOT, Pediatrics **8**:701 (Nov.) 1951.

The history, physical appearance, and laboratory studies performed on eight boys with premature masculinization are presented. The histologic appearance of their testicular tissue is described. Four of the patients had true precocious puberty, which was complete in one and incomplete in three. Four had pseudoprecocious puberty, due to adrenal hyperplasia in three of the patients; two of these had associated metabolic disturbances. In the fourth child pseudoprecocity resulted from an adrenal cortex carcinoma.

Comparison of the two groups of patients shows that physically they are similar, although bilateral enlargement of the testes or metabolic disturbances in some instances may indicate the source of the precocity. The children with adrenal virilism excreted large amounts of 17-ketosteroids, possibly arising from abnormal precursors, while the patients with true precocity excreted only small amounts of 17-ketosteroids. The observations further suggest that testicular biopsy may be a simple additional means of distinguishing between true precocity and adrenal precocity. In the former, the stimulation seems to be all-inclusive with respect to the gonads, leading to the development of large interstitial cells and to tubular maturation and spermatogenic activity of varying degree. In precocity of adrenal origin the interstitial cells do not develop. The appearance of the interstitial cells is apparently the essential feature which differentiates the histology of the testis in these two conditions.

FROM THE AUTHORS' SUMMARY.

UNDESCENDED TESTIS. DOUGLAS MCKAY, Clin. Rep. Adelaide Child. Hosp. **2**:23 (May-Nov.) 1951.

Study of a series of cases has led to the conclusion that true undescended testis is not common. Also, descent spontaneously or following hormonal therapy is not frequent. Gonadotropic hormone should be given in 12 injections between the 8th and 10th year, and, if unsuccessful, operation should be done immediately.

MCGUIGAN, Evanston, Ill.

TERMINAL INTRAMURAL STENOSIS OF THE URETER IN CHILDREN. H. J. BOEVE, Maandschr. kindergeneesk. **18**:258 (Jan.) 1950.

Treatment of terminal intramural stenosis of the ureter in infancy and childhood is discussed.

FROM THE AUTHOR'S SUMMARY.

PAROXYSMAL HEMOGLOBINURIA. YUNG-EN KAO and RAYMOND K. W. YANG, Chinese M. J. **67**:199 (April) 1949.

The authors report two cases of paroxysmal hemoglobinuria, in 14-year-old boys. In both patients symptoms developed after exposure to cold. Both patients had serologic evidence of syphilis. When paroxysmal hemoglobinuria is the only presenting symptom, together with a history of the effect of chilling, then it can be assumed to be associated with a syphilitic infection, particularly the congenital form.

MACDONALD, Pittsburgh.

Diseases of Ductless Glands; Endocrinology

FAILURE OF FOLIC ACID ANTAGONIST TO INTERFERE WITH THE ACTION OF TESTOSTERONE PROPIONATE ON THE COMBS AND TESTES OF YOUNG COCKERELS. M. X. ZARROW, I. B. KORETSKY, and I. G. ZARROW, Endocrinology **48**:125 (Feb.) 1951.

The failure to obtain growth of the female reproductive tract after treatment with estrogen in the absence of folic acid has been well established. The role of folic acid in androgen-induced growth of the male accessories has not been so clearly defined. The experiments here reported indicate that folic acid is not essential for androgen-stimulated comb growth in the cockerel.

JACOBSEN, Buffalo.

EFFECTS OF REPEATED INJECTIONS OF THE STEROIDS AND RELAXIN ON THE SYMPHYSIS PUBIS OF THE GUINEA PIG AS STUDIED BY X-RAY. ROY V. TALMAGE and FERN A. GARRETT, Endocrinology **48**:162 (Feb.) 1951.

It has been known for some time that relaxation of the symphysis pubis of the guinea pig could be brought about by administration of several of the steroids and of extracts containing relaxin, either singly or in combination. These studies can be summed up briefly by saying that estrogen, if given in large enough quantities and for a sufficient period of time, is able to produce separation of the pubes; that relaxin, if administered to an estrogen-primed animal, will cause within a six-hour period a separation of the symphysis which is proportional to the dosage, and that progesterone can indirectly cause relaxation of the symphysis by initiating the production of relaxin from the estrogen-primed uterus. In this paper are given details of experiments further studying this phenomenon as produced by prolonged treatment with estrogen, progesterone, and relaxin.

JACOBSEN, Buffalo.

THE INFLUENCE OF THE THYROID ON CEREBRAL METABOLISM. JOSEPH F. FAZEKAS, F. BURTON GRAVES, and RALPH W. ALMAN, Endocrinology **48**:169 (Feb.) 1951.

The changes in mental activity associated with abnormal thyroid states have usually been explained on the basis of alterations in cerebral metabolism due directly to local excess or deficiency of the thyroid hormone. The studies here reported indicate that cerebral oxygen uptake is not directly influenced by increase or even by decrease of the thyroid hormone.

JACOBSEN, Buffalo.

THE EFFECT OF CORTISONE AND THE ADRENOCORTICOTROPHIC HORMONE OF THE PITUITARY ON THE BLOOD PRESSURE IN EXPERIMENTAL RENAL HYPERTENSION. ARTHUR GROLLMAN and ANDREW KONNERTH, Endocrinology **48**:213 (Feb.) 1951.

The existence of a relationship between the adrenal cortex and the hypertensive state has long been conjectured. The results obtained in this study, as well as the other available data, fail to support the view that hypertension is a result of adrenal cortex or pituitary dysfunction induced by stress or nervous influences.

JACOBSEN, Buffalo.

THE EFFECTS OF CONTINUOUS LIGHT OR DARKNESS ON THYROID FUNCTION IN MICE. G. PUNTRIANO and JOSEPH MEITES, Endocrinology **48**:217 (Feb.) 1951.

Seasonal fluctuations in thyroid function have usually been attributed to temperature changes because of the demonstrated action of heat and cold on thyroid activity. Although the effects of seasonal changes in light increment on thyroid secretion have not yet been investigated, it seems possible that this too may be a factor. Data were obtained which indicate that continuous light depresses and continuous darkness increases thyroid secretion in mice.

JACOBSEN, Buffalo.

THE EFFECT OF SEX HORMONES ON HEPATIC AND RENAL LESIONS INDUCED IN RATS BY A CHOLINE-DEFICIENT DIET. WILLIAM J. EMERSON, PAUL C. ZAMECNIK, and IRA T. NATHANSON, Endocrinology **48**:548 (May) 1951.

The interesting finding of the present experiments is that although estrogens appear to have an ameliorating effect on the production of dietary cirrhosis, androgens have an aggravating effect. The question is raised as to whether it may be worth while to try estrogen as an adjuvant to standard therapy used in the treatment of the early stages of portal cirrhosis in human males.

JACOBSEN, Buffalo.

HYPOTHYROIDISM IN CHILDHOOD. WILLIAM A. REILLY, J. A. M. A. **146**:234 (May 19) 1951.

There are varying degrees of thyroid deficiency. Thyroid deficiency may be more obvious during the rapid spurts in growth in infancy and just before puberty. Clinical observations are more valuable in detecting this deficiency than normal laboratory tests.

KIMBALL, Evanston, Ill.

ALTERATIONS OF CEREBRAL FUNCTIONS IN PHEOCHROMOCYTOMA. N. S. APTER, W. C. HALSTEAD, A. S. ALVING, P. T. TALSO, and T. J. CASE, Neurology **1**:283 (July-Aug.) 1951.

Reports of tumors arising from chromaffin tissue of the adrenal gland (pheochromocytoma) and from ganglia of the sympathetic nervous system (paraganglioma) are being reported with increasing frequency. The pressor substances from these structures discharged into the general circulation produce effects that are of special interest to the neurologist and the psychiatrist. The clinical picture resembles that of anxiety states, vasovagal attacks, and hypothalamic disorders. The syndrome consists of paroxysmal or sustained hypertension, palpitation, sweating, pallor, tremulousness, headache, dyspnea, nausea and vomiting, pain in the precordium and epigastrium, and muscular weakness. Also encountered are vasomotor phenomena, such as discoloration of the hands and legs or blanching of digits, as well as hypermetabolism, glycosuria, amenorrhea, changes in urinary frequency, loss of libido and hyperthermia.

Apter and his colleagues describe combined medical, neurologic, experimental psychologic, electroencephalographic, and psychiatric studies done before and after operation on a patient, aged 14, with pheochromocytoma. These studies revealed that temporary impairment of functions of the cerebral cortex takes place. The generalized systemic vascular changes are accompanied by similar alterations in the cerebral blood vessels and are reversible. These investigators suggest that the somatic experience of anxiety is dissociated from consciousness by virtue of temporary dysfunction of the cerebral cortex.

Preoperative and postoperative electroencephalographic readings showing the effects of piperoxan hydrochloride and epinephrine on the tracings are also recorded.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

PSEUDOHYPOPARATHYROIDISM. M. G. PETERMAN and J. L. GARVEY, Pediatrics **4**:790 (Dec.) 1949.

A typical case of pseudohypoparathyroidism in a 12-year-old girl is presented. The history alone was typical of hypoparathyroidism. Physical examination revealed a characteristic round, full face in a short plump girl with positive facial, ulnar, and peroneal reflexes. The serum

calcium was low, the serum phosphorus high, and the urinary phosphorus excretion was low. Injection of parathyroid extract intravenously produced an increased urinary excretion of phosphorus. An unusual feature of this case was the demineralization of all the bones.

FROM THE AUTHORS' SUMMARY.

THYROID DEFICIENCY IN CHILDHOOD. WILLIAM A. REILLY, South. M. J. **44**:200 (March) 1951.

A review of the clinical picture and the differential diagnosis is presented. The need for early diagnosis is emphasized, because good mental development depends on the early institution of adequate treatment. About 20 to 25% (presumably of cretins) attain fairly normal mentality if treatment is started early.

LOGAN, Rochester, Minn.

PUBERAL DEVELOPMENT OF SUBJECTS WHO HAD HAD ENLARGED THYMUS GLANDS IN INFANCY. A. BARCAGLIA, Minerva pediat. **2**:222 (May) 1950.

Some of the 30 subjects, who had had enlarged thymus glands in infancy, had had lymphatism, and some had had x-ray treatments. No effect could be established at puberty related to previous symptoms of lymphatism or to x-ray therapy. Puberal evolution was essentially normal in all cases, although four subjects may have been a bit precocious and one delayed. Somatic development was normal, although one half the subjects were somewhat overweight and one was rather tall. Genital growth was normal. None showed Froehlich's syndrome.

HIGGINS, Boston.

THERAPEUTIC RESULTS IN HYPOPHYSIAL INFANTILISM. ROSA B. DE BUÑO, Arch. pediat. Uruguay **21**:908 (Nov.) 1950.

Seven cases of hypophysial infantilism, observed for periods varying from 1 to 6 years, have been studied. The results obtained with different therapies in this disease are analyzed. Changes in stature and bone growth, in the genital tract, and in sexual characteristics are studied particularly, because of their extreme interest. Attention is called to the importance of gonadotropins in the treatment of male sexual infantilism and of androgens in the effect on growth. Androgens have proved to be, up to now, the most favorable element for stature growth.

FROM THE AUTHOR'S SUMMARY.

BODY UNDERDEVELOPMENT IN DIABETES MELLITUS. ODDVAR ANDRUP, Tidsskr. norske lægefor. **70**:577 (Sept. 15) 1950.

Of 51 children with diabetes, aged 2 to 12 years, treated in 1935 to 1949, there were 13 (8 boys and 5 girls) who were classified as dwarfs. The dwarfism was of pituitary type except in one girl who displayed signs of hypothyroidism.

WALLGREN, Stockholm, Sweden.

THE CORTICOTROPE HORMONE. J. W. R. EVERSE, Nederl. tijdschr. geneesk. **94**:2058 (July 22) 1950.

Remarkable effects of corticotropin (ACTH) are observed in widely different diseases. In a few diseases only distinct therapeutic effects were obtained.

The dosages used, especially in the United States, seem rather high. The practice of expressing the dosage in milligrams actually only indicates the dosage of a particular preparation. As yet, an international standard preparation does not exist. Preparations of American or Dutch origin are verified, however, with respect to standard preparations of equal concentrations.

VAN CREVELD, Amsterdam, Netherlands.

ADRENOCORTICOTROPE HORMONE (ACTH) AND CARBOHYDRATE-METABOLISM. G. A. OVERBEEK, Nederl. tijdschr. geneesk. **94**:2526 (Sept. 2) 1950.

From a consideration of the action mechanism of corticotropin (ACTH) and from experiments on animals, the author concludes that the danger of corticotropin therapy causing real diabetes is very small. Only if a light diabetes already exists is there a certain possibility of deterioration.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

APPEARANCE OF CENTERS OF OSSIFICATION IN THE HUMAN PELVIS BEFORE BIRTH. CARL C. FRANCIS, Am. J. Roentgenol. **65**:778 (May) 1951.

This article describes the appearance of the ossification centers of the pelvis with respect to crown-to-buttocks length of the fetus. Tables are presented showing the appearance of ossification centers in the ilium, ischium, pubis, centra of the sacral vertebrae, transverse processes of the sacral vertebrae, lateral sacral centers, and coccygeal centers.

HODGSON, Rochester, Minn.

GROWTH OF THE SHAFT OF THE HUMAN RADIUS AND ULNA DURING THE FIRST 2 YEARS OF LIFE. MUSA K. GHANTUS, Am. J. Roentgenol. **65**:784 (May) 1951.

The average length of the shaft of the radius and ulna was determined by measuring these bones at the ages of 3, 9, 12, 18, and 24 months. The average rate of growth was calculated and was found to be greater in boys during the first year and greater in girls during the second year.

HODGSON, Rochester, Minn.

INFANTILE CORTICAL HYPEROSTOSIS: A FAMILIAL DISEASE? JAMES G. BOYES, and NICHOLAS G. DEMY, Am. J. Roentgenol. **65**:924 (June) 1951.

The cause of infantile cortical hyperostosis is still unknown. The manifestations of the disease consist of doughy swellings, irritability, and tenderness, with cortical overgrowth apparent in roentgenograms. The authors present the cases of a brother and sister with the disease and suggest the possibility of a familial incidence.

HODGSON, Rochester, Minn.

SACROCOCCYGEAL TERATOMA IN THE NEWBORN. JOSEPH M. WALKER, and ROBERT J. P. FOSTER, Arch. Surg. **61**:1138 (Dec.) 1950.

Sacrococcygeal teratomas are usually obvious at birth but may vary in manifestations from a small discoloration on the buttocks to a large sacrococcygeal mass which causes dystocia or even fetal death. The symptomatology depends on the location and size of the teratoma. Immediate surgical removal of the tumor is indicated, because the rate of growth is usually rapid and the skin undergoes necrosis and becomes infected. A case of sacrococcygeal teratoma is reported.

KAISER, Rochester, N. Y.

MYASTHENIA GRAVIS IN A MOTHER AND HER NEWBORN SON. G. E. MCKEEVER, J. A. M. A. **147**:320 (Sept. 22) 1951.

McKeever describes the seventh known case of myasthenia gravis occurring in a newborn child of a myasthenic mother.

The outstanding features of the case of myasthenia gravis in the mother were as follows: (1) The unusual nature of the patient's initial symptoms had allowed the disease to go undetected for 16 months; (2) the patient experienced a remission during the first five months of pregnancy; (3) a relapse occurred during the sixth month of pregnancy; (4) a remission occurred on the day of delivery; (5) a relapse followed the delivery and, in turn, was followed by a remission; (6) the baby was delivered by Caesarean section, for reasons not related to the myasthenia gravis.

The outstanding features of the case of myasthenia gravis in the baby were as follows: (1) The baby was normal at birth; (2) the symptoms of myasthenia developed gradually from birth, so that they were clearly recognized by the second day of life; (3) the diagnosis was easily proved by oral administration of neostigmine bromide; (4) the baby required no neostigmine after 15 days of life.

McKeever points out that the transient nature of myasthenia in newborn infants should not cause the clinician to consider the problem lightly. Two deaths have been reported in this series of seven cases.

The mechanism of the transient myasthenia in the baby here described and in others is a matter of conjecture. It is certainly related to the mother's illness. It may be postulated that there exists an increase in cholinesterase in the infant. This may be a reflection of increased circulating cholinesterase in the mother. It is also possible that an increase in circulating cholinesterase developed in the baby in response to the neostigmine medication administered to the mother. The latter possibility is more likely, since the baby was well at birth and the symptoms of myasthenia developed in progressive severity several hours after birth. If the increased cholinesterase of the baby were only a reflection of the increased cholinesterase of the mother, it would be expected that the myasthenia would be severest at birth and show progressive improvement. No case of myasthenia gravis in infancy had been observed prior to the introduction of neostigmine (prostigmin®) in 1935.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

EPIPHYSEAL INJURIES IN BREECH DELIVERY. BERNARD H. SHULMAN and CHARLES D. TERHUNE, Pediatrics **8**:693 (Nov.) 1951.

During the course of breech extraction or breech presentation with version and extraction, injury to the extremities may be a complication. Trauma and separation of an epiphysis, with or without apparent dislocation, may occur. When this involves the upper or lower femoral epiphysis, a sequence of changes takes place which forms a characteristic clinical and pathologic picture. There is usually no hint of injury until the second day of life when the infant assumes the "frog position," with the affected extremity held flexed at the knee and hip and externally rotated. The soft tissue over the involved area is full, tense, and often reddened. There is marked tenderness and pain on passive motion. The patient is extremely irritable and may run a low-grade temperature. Roentgenograms, which are normal for about the first five days, begin to show subperiosteal changes indicating local calcification of extravasated blood at the site of the injury.

A similar picture prevails when the injury involves the upper extremity. In this instance the affected limb is held limp, extended, and externally rotated. There is pain on motion. The injury usually involves the upper humoral epiphysis, and there is overlying soft-tissue swelling, with alteration of the normal shoulder contour. Roentgenographic changes follow the same pattern as those for the lower extremity.

The mechanism of these injuries seems to resolve itself into the position of stress and strain. During delivery or decomposition of the presenting breech, manipulation of the extremities is necessary.

The underlying pathology consists of periosteal stripping, starting at the epiphyseal line and extending as far as the opposite end of the involved bone. The resultant hemorrhage lifts up the periosteum, and ultimately this subperiosteal extravasation results in the clinical picture described. By the fifth day callus replaces the hemorrhage, and roentgenograms begin to reveal the calcium-containing healing process, often appearing as an ossifying periostotic sleeve. By the time there is roentgenographic evidence of callus formation, the clinical picture improves, and there is beginning painless motion of the affected limb.

The relationship of maternal parity to epiphysial injury in breech extractions seems to be an intimate one. One may infer that the unyielding soft parts of a primiparous mother, in the presence of a breech presentation, add to the difficulties of delivery and necessitate the application of additional force and pull on the part of the attending physician.

Four cases of epiphyseal birth injuries in direct or altered breech extractions are presented in detail.

FROM THE AUTHORS' SUMMARY.

THE GENERALIZED DEVELOPMENTAL OSSEOUS DYSTROPHIES: INTRODUCTORY CLASSIFICATION: 1. MULTIPLE EXOSTOSES. W. P. U. JACKSON, South African M. J. **25**:334 (May 19) 1951.

After outlining a clinical classification of osseous dystrophies, the author discusses very briefly the problem of multiple exostoses.

McGUIGAN, Evanston, Ill.

THE GENERALIZED DEVELOPMENTAL OSSEOUS DYSTROPHIES: 2. ACHONDROPLASIA. W. P. U. JACKSON, South African M. J. **25**:350 (May 26) 1951.

This is the second in a series of papers on osseous dystrophies. The author gives a very brief discussion.

McGUIGAN, Evanston, Ill.

THE GENERALIZED DEVELOPMENTAL OSSEOUS DYSTROPHIES: 6. OSTEOGENESIS IMPERFECTA. W. P. U. JACKSON, South African M. J. **25**:433 (June 23) 1951.

This is the sixth in a series of articles on generalized osseous dystrophies. The author discusses briefly the disease of osteogenesis imperfecta.

McGUIGAN, Evanston, Ill.

THE GENERALIZED DEVELOPMENTAL OSSEOUS DYSTROPHIES: 7. OSTEOPETROSIS. W. P. U. JACKSON, South African M. J. **25**:451 (June 30) 1951.

The syndrome of osteopetrosis is discussed in a very brief article forming the seventh of a series of papers on generalized developmental osseous dystrophies.

McGUIGAN, Evanston, Ill.

SO-CALLED CAT SCRATCH DISEASE, A BENIGN VIRUS LYMPHADENITIS. T. WEGMANN, C. USTERI, and C. HEDINGER, Schweiz. med. Wchnschr. **81**:853 (Sept. 8) 1951.

Thirty cases of cat scratch disease (cat scratch fever) are tabulated, 10 of which occurred in children 2 to 14 years old. In 26 cases a contact with cats was noted. The disease can occur even when such a contact can be excluded. So-called cat scratch disease is characterized by subacute or chronic lymphadenitis. Local manifestations are the most prominent symptoms. Systemic reactions are rather insignificant. A granulomatous inflammation of lymph nodes, with abscess formation, constitutes the pathological lesion. It is usually confined to a single location. In all probaility a virus closely related to that of lymphogranuloma venereum is responsible for the disease. The incubation period may possibly vary from five days to six weeks. The diagnosis can be certified by a skin test with diluted sterile pus from a node. The reaction becomes positive one month after infection and remains so for years. The differential diagnosis is discussed. Special therapeutic measures are not necessary. Puncture or excision of the nodes may hasten recovery. Treatment with aureomycin or terramycin has been recommended.

AMBERG, Rochester, Minn.

PRESENT STATUS OF CONGENITAL DISLOCATION OF THE HIP. M. ORTOLANI, Minerva pediat. **3**:453 (Aug.) 1951.

For the past 30 years the author and Putti have been making appeals for early diagnosis of congenital dislocation of the hip. In some sections of Italy, the incidence of lameness in adolescents and adults due to this condition has markedly diminished; but in other sections the incidence has not changed. Italian orthopedists do not resort to such radical treatment as do orthopedists in Western Europe and America, but, in any event, early diagnosis and treatment is imperative for best end-results.

HIGGINS, Boston.

OSTEOPETROSIS. E. TOUSSAINT ARAGON, Bol. med. Hosp. inf., México **7**:846 (Dec.) 1950.

The author reports 3 cases of marble bones, or osteopetrosis, affecting 3 children who were admitted to the Hospital Infantil. Two were brothers aged 13 and 12 years; the other was an infant 6 months old. The general characteristics of the disease are discussed briefly. The clinical histories are summarized, stressing especially the modifications found by roentgenographic study. Because of its rarity, the third case is of special interest, since it includes both osteopetrosis and rickets.

FROM THE AUTHOR'S SUMMARY.

TREATMENT OF POLYMYOSITIS WITH PENICILLIN. F. H. DOST, Arch. Kinderh. **140**:183 (No. 4) 1950.

A description and discussion of polymyositis in a 12-year-old boy is given. Skin biopsy affirmed the clinical diagnosis. There was no response to treatment with sulfonamides, but favorable results followed the administration of 3,000,000 I.U. of penicillin over a period of two weeks.

GOTTSTEIN, Chicago.

News and Comment

GENERAL NEWS

Specialists Certified by American Board of Pediatrics, Inc.—The following physicians were certified as specialists by the American Board of Pediatrics, Inc., after examinations held in Washington, D. C., May 2, 3, and 4, 1952:

Adams, Frederick F., Jr., Spartanburg, S. C.
Armstrong, William Bennett, Fargo, N. D.
Arnold, Herbert L., Jr., Tuscaloosa, Ala.
Baggs, Wade, H., Jr., Tampa, Fla.
Baldwin, Ruth Workman, Baltimore.
Blinski, Maurice, Miami, Fla.
Bost, Roger Browning, New Orleans.
Brandt, Ira Kive, Coral Gables, Fla.
Bruch, William M., Bluefield, W. Va.
Butler, Robert Elliott, Rochester, N. Y.
Chasler, Nicholas Louis, Pittsburgh.
Childs, Barton, Baltimore.
Chisolm, James Julian, Jr., Baltimore.
Cohlan, Sidney Q., New York.
Crane, Norman T., Plainfield, N. J.
Crawley, Eugene Harvey, Little Rock, Ark.
Dick, James, Hempstead, N. Y.
Dougan, Hubert Taylor, Richmond, Va.
Epstein, Nathan, Philadelphia.
Eriksen, George Norton, Jr., Wilmington, Del.
Finberg, Laurence, Baltimore.
Frazier, Claude Albee, Asheville, N. C.
Graub, Milton, Philadelphia.
Greenspan, Herbert S., Philadelphia.
Harris, Irwin Lee, Far Rockaway, N. Y.
Harris, Robert Otis, III, Mobile, Ala.
Jackson, Harold Pryor, Anderson, S. C.
Jenkins, Melvin Earl, Jr., Washington, D. C.
Joseph, Clifford, Torrington, Conn.
Kahn, Robert Edward, Baltimore.
Karzon, David Theodore, New York.
Kravis, Lillian B. Panzer, Philadelphia.
Lace, Richard Edward, Tarentum, Pa.
Lippi, Frank Antonio, Jr., Philadelphia.
Luhby, Adrian Leonard, New York.
Lyles, Clarence Cross, Spartanburg, S. C.
Lynch, John Franklin, Jr., High Point, N. C.
McGovern, John Phillip, Silver Spring, Md.
McLeod, Robert Nall, Jr., Somerset, Ky.
McPherson, Thomas Coatsworth, Atlanta.
Myers, Morris, Flushing, N. Y.
Nichols, Myron McCall, Charlottesville, Va.
Ogborn, Richard Eugene, Fort Bragg, N. C.
Olshaker, Bennett, Washington, D. C.
O'Rear, Harry Barron, Augusta, Ga.
O'Reilly, Philip Joseph, Mamaroneck, N. Y.
O'Shea, James Arthur, Andover, Mass.
Parrish, Wilmer Eugene, Longview, Tex.
Perry, Douglas Dards, Bristol, Conn.
Pfeifer, Robert Thomas, Media, Pa.
Potterfield, Thomas Garland, Charleston, W. Va.
Prentice, Stanley Edward, Tenafly, N. J.
Rauber, Albert Paul, Decatur, Ga.
Riepenhoff, John Patrick, Columbus, O.
Rosen, Sydney Irving, Ontario, Canada
Rosenblum, Herman, Nashville, Tenn.
Ross, Lucille Jaffe, New York.
Seidel, Henry Murray, Baltimore.
Seiler, William Carpenter, Sandusky, O.
Skinner, Richard Greene, Jr., Jacksonville, Fla.
Small, Leon I., Millburn, N. J.
Smith, Alan Eugene, Cleveland.
Smith, Martin Henry, Gainesville, Ga.
Steinburg, Stanley Herbert, Washington, D. C.
Tilley, John Allen, Red Bank, N. J.
Vargas, Dharma Luz, Rio Piedras, P. R.
Waldman, Sydney, Philadelphia.
Walker, Lewis Harry, Akron, O.
Weber, John Richard, Fort Wayne, Ind.
Weyland, Charletta Kathern, Lebanon, Pa.
Woodruff, Calvin Watts, Nashville, Tenn.
Young, Latimer Gorsuch, Baltimore.
Zupanc, Edward, Lt. (jg) (MC), U.S.N.R., Great Lakes, Ill.

Inauguration of the Sweet Lectureship.—Dr. Clifford Sweet, for 30 years chief of staff of Children's Hospital of the East Bay in Oakland, Calif., was honored by the medical staff there on May 21, 22, and 23, with the inauguration of the "Clifford Sweet Clinics and Lectureship."

Monograph on Plasma Proteins.—The monograph "Physiological Changes in Plasma Proteins Characteristic of Human Reproduction" was produced to make the results of electrophoretic studies of blood plasma proteins carried out by the Research Laboratory of the Children's Fund of Michigan available in more complete form than is possible in journals. Copies are available for free distribution to workers in this field.

PERSONAL NEWS

Faculty Changes at Louisiana State University.—Dr. Myron E. Wegman, Professor and Head of the Department of Pediatrics at Louisiana State University, School of Medicine, and Pediatrician-in-Chief of the Louisiana State University Unit at Charity Hospital of Louisiana at New Orleans, has resigned these positions to accept appointment as Director of the Division of Education and Training of the Pan American Sanitary Bureau, the Regional Office of the World Health Organization for the Americas. Dr. Nelson K. Ordway, at present Associate Professor of Pediatrics at Louisiana State University, will succeed Dr. Wegman.

ANNOUNCEMENTS

Society for Pediatric Research.—The Society for Pediatric Research held its meeting on May 5, 6, and 7, 1952, at Old Point Comfort, Va. The following officers were elected to serve for the year 1952-1953: President, Dr. Robert Ward, New York; Vice-President, Dr. Milton Rapoport, Philadelphia; Secretary-Treasurer, Dr. Sydney Gellis, Boston; Members of the Council, Dr. Edward Pratt, New York; Dr. Nelson Ordway, New Orleans; Dr. Charles May, Minneapolis; Dr. Gladys Fashena, Dallas, Tex.; Dr. Herbert Miller, Kansas City, Kan., and Dr. John F. McCreary, Toronto, Canada. The following were elected to membership in the Society: Robert Aldrich, Portland, Ore.; Barton Childs, Baltimore; John F. Damman, Santa Monica, Calif.; Floyd W. Denny, Minneapolis; Lloyd J. Filer, Rochester, N. Y.; Gordon E. Gibbs, Baltimore; David Gitlin, Boston; Bruce D. Graham, Ann Arbor, Mich.; Robert H. High, Philadelphia; Solomon A. Kaplan, Cincinnati; Gerald Miller, Rochester, N. Y.; Frederick C. Moll, Seattle; Erwin Neter, Buffalo; William Obrinsky, New Orleans; James J. Quilligan, Dallas, Texas; Helen S. Reardon, Philadelphia; Andrew J. Rhodes, Toronto, Canada; Irving Schulman, New York; Roland B. Scott, Washington, D. C., and Edna H. Sobel, Cincinnati.

Books

Handbook of Pediatric Medical Emergencies. By Adolph G. De Sanctis, M.D., and Charles Varga, M.D. Price, $5. Pp. 284, with 51 figures, 13 tables, and 4 appendix tables. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

This handbook was originally written for the use of the resident staff and for physicians enrolled in the courses offered by the pediatrics department of the Post-Graduate Medical School of New York University-Bellevue Medical Center.

It has now been enlarged and revised for general publication. Because of its wealth of readily utilized information, it will, no doubt, soon be a standard reference for the practicing pediatrician and general practitioner, as well as for pediatric hospital staffs and hospital emergency departments.

The handbook is divided into ten chapters, an addendum, and an appendix.

The chapter on cardiovascular emergencies covers acute cardiac failure, arrhythmias, and pericardial effusion.

Under the heading of gastrointestinal emergencies, the treatment of acute toxic diarrhea is well covered, and this section includes a helpful table of electrolyte contents of replacement solutions, with comments as to their uses.

The chapter on genitourinary emergencies is short but covers anuria, injuries, renal colic, and foreign bodies.

The chapter on neurological emergencies contains a very complete section on the treatment of convulsions. The treatment of diabetic coma is also included in this chapter.

Under respiratory emergencies, croup, asthma, acute bronchiolitis, and resuscitation of the newborn infant are given full consideration from the standpoint of therapy.

The various methods of resuscitation are described and discussed in the chapter on drowning.

In the chapter on poisoning the signs and symptoms are given for only a few of the poisons mentioned. A long and very complete list of antidotes to be kept on hand in the hospital emergency room is given. The treatment given is definite, with doses and percentages clearly given. This is a distinct improvement over many such sections in textbooks where the treatment is given only in general terms, wasting precious time in an emergency while the physician looks up the dosage elsewhere.

Important and helpful also is a list of nearly five hundred commercial sources of poisons listed by their brand names, with the poisonous ingredient of each. Such a list has long been needed by medical practitioners in order that it may be determined just what poison is being dealt with when a household substance or insecticide has been ingested. The list would be even more helpful if the percentages of the poisons were given, and if it was made a part of the chapter on poisoning instead of being placed at the end of the book as an appendix.

The care of the premature infant is well covered from the emergency standpoint.

The section on miscellaneous emergencies lists the treatment of various types of bites, burns, electric shock, eye injuries, frostbite, heat exhaustion, and serum reactions.

The last chapter is on pediatric procedures. This is well illustrated with photographs and drawings. Explained in detail are various types of venipuncture, constant drip technique, lumbar puncture, subdural tap, tracheotomy, and oxygen and aerosol therapy.

Additional information relating to several of the chapters is given in an addendum. This is confusing and detracts from the value of the book. It is hoped that an early revision will correct this fault.

A useful table of normal physical and chemical constants is given in the appendix, as well as the list of poisons already mentioned.

This book is highly recommended to all practitioners and house officers who treat the medical emergencies of children.

Pharmacological Basis of Penicillin Therapy. By Karl H. Beyer, M.D. Price $4.50. Pp. 214, with 35 illustrations. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

"The purpose of this monograph has been to present briefly the pharmacological basis of penicillin therapy in a concise and reasonably complete form." This is the introductory sentence in the preface, and the word "clearly" could well have been added. The text is preceded by an excellent table of contents which gives the reader, in a very few minutes, a clear idea of the subject, and each of the seven chapters is introduced by a summary of less than a page of fine print.

The first two chapters discuss the absorption, distribution, concentration, and elimination of penicillin into the various fluids, tissues, organs, and cavities of the body when given by various channels, i. e., orally, subcutaneously, intravenously, etc.

Chapter III introduces the clinical phase of the subject, and when one bears in mind the wide variation in the natural course of most human illnesses, one understands the difficulties in assessing the various methods of administering penicillin and the results from different schedules of injection, blood levels, etc. These factors are clearly presented and explained, and three quotations illustrate these points.

"Blood levels of penicillin are of inestimable value but they give no great assurance that one is attaining the same antibiotic concentration of the agent within the site of pathology, except where that is represented by a septicemia. . . . There is good agreement between both schools of thought that penicillin blood levels may fall below detectable amounts temporarily without adverse effects on the outcome of therapy. . . . . There have been several experimental and clinical papers that indicate the total penicillin dose may be divided into large increments administered at long intervals with at least as good results as when the daily dose was divided into small increments injected frequently."

Chapter IV should be of interest to all practicing pediatricians, since it presents the data on repository penicillin preparations. It would seem that these are narrowing down to products which seldom result in induration at the injection site. Specifically, the crystalline-procaine-penicillin-with-aluminum-monostearate group seems very efficacious, also the mixture of penicillin sodium with penicillin procaine administered intramuscularly.

The following chapters are devoted chiefly to the physiology of penicillin elimination by the kidneys, both by tubular secretion and by glomerular filtration, and the great inhibiting action of the tubular secretion by carinamide (originally caronamide). Carinamide is readily absorbed when administered orally and is relatively unlikely to result in side reactions, but the authors point out that it is precipitated from acid urine and may suggest proteinuria to the uninitiated. Its chief use, as is well known, is the maintenance of a very high penicillin blood level in bacterial endocarditis and in other infections in which a high level is necessary for penetration of penicillin to the indurated area. "In the therapy of penicillin-sensitive infections where oral penicillin has been shown to be effective when administered in high dosages, the coadministration of carinamide would be expected to reduce the necessary unitage of penicillin or increase the antibiotic tissue concentrations." The maximal oral dose of carinamide recommended is 2 to 4 gm. every three or four hours for adults. The dosage recommended (quoted by the author) for infants and children varies from 0.4 to 0.8 gm. per kilogram per day. This is relatively much larger than that for adults, but when one has repeatedly seen the adult dose (300,000) of penicillin given to small infants by pediatricians one can understand this discrepancy.

Therapeutics in Internal Medicine. Edited by Franklin A. Kyser, M.D. Price, $12.00. Pp. 715, with numerous tables. Thos. Nelson & Sons, Cape Wood and Davis Sts., Camden, N. J., 1950.

This volume is prepared by 82 contributors. Dr. Kyser is a practicing physician and a member of the teaching staff of Northwestern University and the Evanston Hospital. Each of the contributors is a recognized authority, and most of them are practitioners, which is an indication of the effort made to present a practical book. The book deals only with treatment and is presented in the what-when-and-how fashion. In all, there are 268 articles.

In general, the book is very adequate, well presented, and up to date. Sections of particular interest to pediatricians are well done. There are some statements which might be criticized and

some unnecessary omissions, but not too many. The infectious diseases are adequately handled. Not much is said of the use of chloramphenicol against pertussis. In scarlet fever, penicillin is advocated over the sulfonamides, and the statement is made that the sulfonamides are best used in conjunction with scarlet fever convalescent serum. It is believed that for children sulfonamides are often superior to penicillin in dealing with hemolytic Streptococcus infections. Nothing is said of the use of sulfonamides prophylactically.

In the discussion on pneumonias, the following suggestion is also impractical. "Smears and cultures of the nose, throat and sputum and a leukocyte count are prerequisite to proper management of all respiratory infections, whether pneumonia has developed or not. If these reveal large numbers of pneumococci, hemolytic streptococci, or if Streptococcus viridans is found in the nose, or if there is a high leukocytosis, the indication for sulfonamide or penicillin in full doses is clear. Hemophilus influenzae and Klebsiella pneumoniae infections of the respiratory tract may respond better to streptomycin."

In the discussion of the treatment of leprosy, no mention is made of streptomycin. The treatment in infantile atopic eczema is the same as has been used for decades, none of which has done much to alleviate this condition. Impetigo is still treated with ammoniated mercury ointment and methylrosaniline chloride.

All in all, it was a pleasure to read this book. Many sections are very well done, those on the meningitides, metabolic diseases, and cardiovascular and renal diseases, to mention a few. The book is new and up to date. It should be a valuable aid to the busy practitioner who wants to find information quickly and in a condensed form but still clearly and understandably presented.

Food Allergy. By Herbert J. Rinkel, M.D. Price, $8.50. Pp. 492, with 22 illustrations and a few food tables. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

This book presents a very interesting and unique approach to the diagnosis of food allergy. Not too much credence is given to skin tests as diagnostic criteria for allergies to foods. Perhaps this is justified in adults because food allergy in adults is widely known for the false-positive skin reactions that are elicited. This is due to two factors: First, when the intracutaneous method is used, false reactions, particularly to vegetables and fruits, are often elicited, and second, a residual skin hypersensitivity may be present in a person who may have complete clinical tolerance for that food.

The diagnosis of food allergy by this author is divided into a number of phases which seem bewildering. According to him, a person may show one of many reactions to foods: complete absence of reaction, masked reaction, immediate reaction or even reactions to foods one to several days later. Such a state of affairs would lead to many subjective interpretations. In a sense, all persons tested under such criteria would, through clinical trials, undoubtedly fit into one or another of these groups.

The second half of the book, devoted to recipes and the ingredients of various brand foods, is valuable.

One cannot escape the conclusion that the concept of food allergy presented here is definitely linked with psychic factors which, for one or another reason, have made the patient subjectively intolerant to certain foods. To call such cases allergic is not entirely justified.

From the standpoint of clinical allergy in childhood, the whole approach appears to be entirely too complicated for ready application in pediatrics. It is therefore believed that this book is more suited for highly trained allergists dealing with adults.

Progressive Resistance Exercise. By Thomas L. DeLorme, M.D., and Arthur L. Watkins, M.D. Price, $5.00. Pp. 245, with 89 figures and 13 tables. Appleton-Century-Crofts Company, Inc., 35 W. 32d St., New York 1, 1951.

Progressive resistance exercise is a method of strength and muscle building which has been developed by trial and error methods and used by weight lifters for many years. The enormous muscle development which these men achieve is well known. The use of this principle in the treatment of pathological conditions was begun during World War II and has proved to be the most important advance in recent years in the restoration of injured and diseased joints to good function. It has also been very useful in building up muscles weakened by poliomyelitis and

certain other neuromuscular diseases. This book offers for the first time, in a concise, well-organized, and complete form, about all that is known of this method as it is used in modern physical therapy.

The authors have used excellent judgment in giving a great deal of space to techniques, illustrating each in such a clear manner that the book becomes a most practical manual for specialists in physical therapy. The physiological background for each joint or disease entity is presented, in addition to chapters on the general physiology and principles involved. Lengthy and tedious technical data have wisely been omitted, with the result that most readers will find it profitable to read this book from cover to cover. The proper use of progressive resistance exercises should be familiar to all specialists in physical therapy and to physicians who treat neuromuscular and joint pathology, and this book may be highly recommended to them.

Cancer As I See It. By Henry W. Abelman, M.D. Price, $2.75. Pp. 100. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1951.

The author believes that infection is the cause of cancer, and this book, as the title indicates, is an explanation of why he holds this theory. More specifically, he attempts to identify the infecting agent as "the mold fungus, an organism capable of modifying its form and properties when subjected to a change in environment." He considers that the pleomorphism of this organism acting in different tissues is responsible for the development of "carcinoma, sarcoma, pernicious anemia, leukemia, Paget's Disease, rodent ulcer . . . cancer granuloma, Hodgkin's Disease, and mycosis fungoides." He believes that heredity plays an important role and that, in addition to the "mold or fungus," a devitalizing agent to reduce cellular resistance to invasion is also essential.

Among the studies being pursued to determine the cause or causes of cancer, investigations on micro-organisms have long occupied an important position. Whether or not human cancers have infectious agents as necessary components in their etiology remains to be proved. That there are suggestions of such a cause in certain tumors no one will deny. The author, however, has assumed a strangely uncompromising attitude for a serious student of pathology, particularly since his own "researches" and supporting references are undocumented.

The tone of the text is likewise argumentative, declamatory, and occasionally scolding, rather than objective.

The uncritical lay reader may be misled by many of the statements in this book, and the inquiring physician will find no stimulation in it.

Bacterial Polysaccharides. By Martin Burger. Price, $6.00. Pp. 254, with 48 tables. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

This monograph is concerned principally with the polysaccharides of pathogenic bacteria. The discussion is divided into chapters, in each of which there is a condensed review of the literature pertaining to polysaccharides isolated from related types of bacteria. Each chapter begins with an introductory or historical section. This is followed by sections dealing with isolation, properties, and uses of the polysaccharides. Details concerning procedures for isolation are given in an appendix at the end of the monograph. Emphasis, however, is placed upon immunologic properties rather than upon physicochemical properties of the polysaccharides. In each instance, care is taken to point out the therapeutic and prognostic advantages gained by studies in this field of immunology. Each chapter is terminated by a large number of appropriate references to the literature. The impression is gained that interest in intensive investigation of bacterial polysaccharides subsided as antibiotic and chemotherapeutic drugs were developed. It is hoped that this monograph will be of assistance in reorientation of immunologists to the fundamental aspects of infection and immunity.

Contribución al estudio del rabdomioblastoma. By Ramiro Alvarez Zamora. Price, 50 pesetas. Pp. 82, with 18 illustrations. Librería De Ciencias Médicas, Barcelona, Spain, 1950.

In this very excellent monograph on rhabdomyoblastoma the author has analyzed 72 cases from the medical literature and added 3 of his own. These "mixed tumor" sarcomas appear in the first two years of life on the anterior wall of the vagina. Their growth is continuous toward

the exterior, and in time they metastasize into the softer surrounding tissues. They cause urinary difficulties that lead to hydronephrosis.

A new approach has been made by the author in histological differentiation of these cells as immature striated muscular elements. The prognosis is bad unless early treatment by extirpation of the tumor and adjacent tissue is made, with further radium treatment. Of all the known cases, in only three did the patients survive after 15 years of observation.

Although written in Spanish, this monograph is very easily understood, as the diagrams and plates are excellent. The bibliography is well chosen. This is a very complete and thorough study of the subject.

Virus and Rickettsial Diseases. By S. W. Bedson, A. W. Downie, F. O. MacCallum, and C. H. Stuart-Harris. Price, $5.50. Pp. 383, with 33 figures and 5 tables. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1951.

This is an excellent book and can be highly recommended. It should be especially valuable as a concise reference for recent opinion regarding the nature of the virus and the epidemiology of virus and rickettsial disease. The authors are internationally known British authorities and write with their usual clarity. Of particular interest are the introductory chapters by Prof. Bedson on immunity and pathogenesis. The animal origin of viral and rickettsial disease, with all its implications, is emphasized. The specific diseases are covered in individual chapters by the other authors. Only brief mention is made of the clinical characteristics, which allows more space to be devoted to the aspects of disease in which there has been recent progress. The sections on laboratory diagnosis are particularly complete. This volume will be of particular interest to students, investigators, and teachers. However, the practicing physician should read this book to bring himself up to date on modern aspects of these infectious diseases.

La obesidad en la infancia. By Perlina Winocur. Price, not given. Pp. 59, with 7 tables and 7 graphs. El Ateneo, Córdoba 2099, Buenos Aires, Argentina, 1950.

The author classifies obesity in children into two large groups: (*a*) simple obesity, due to constitution or alimentation (exogenous), and (*b*) obesity accompanied with other disorders, such as pituitary, genital, suprarenal, and thyroid deficiency. These phases are discussed in detail by means of case histories, tables, and graphs. Various forms of treatment are analyzed, and a chapter is devoted to prophylaxis.

This is a well organized and readable little volume written in Spanish. An excellent biography is included.

Trephine Technique of Bone Marrow Infusions and Tissue Biopsies. Third edition. By Henry Turkel, M.D. Price, not given. Pp. 60, with 30 illustrations. Gale Printing Company, 1036 Beaubien, Detroit, 1950.

This is the third edition of this compact little book. It contains all the material in the former editions, with revised techniques and with the bibliography brought up to date.

The purpose of the book is to present to the medical profession a booklet which provides the fundamentals of bone-marrow infusion and simplified procedures for making diagnoses by means of tissue biopsy. All the methods are well illustrated by adequate drawings.

Good Food for Diabetics. By Eleanor Record Sigel. Price, $2.50. Pp. 144, with numerous daily diet charts. Harper & Brothers, 49 E. 33d St., New York 16, 1951.

The author of this book has given some specific directions on (1) things to remember, (2) menus, and (3) meat recipes, including food for diabetics and desserts for the rest of the family. The recipes are different and interesting, and, judged by their description, the author is not only an excellent dietitian but also a qualified cook.

Directory of Pediatric Societies *

INTERNATIONAL

International Union for Child Welfare

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 16, rue du Mont-Blanc, Geneva, Switzerland.
Place: Bombay, India. Time: Dec. 5-12, 1952.

IV° Congreso Panamericano de Pediatria, American Academy of Pediatrics

President: Dr. João Mello Teixeira.
Secretariat: Rua Dias da Rocha 25, ap. 602, Copacabana, Rio de Janeiro.
Place. Rio de Janeiro. Time: 1954.

IV° Congreso Sudamericano de Pediatria, Confederacion Sudamericano de Sociedades de Pediatria

President: Dr. Jose Magalhaes Carvalho.
Secretary: Dr. Afranio Raul Garcia.
Place: Avenida Mem de Sá 197, Rio de Janeiro. Time: 1954.

FOREIGN

Academy of Medicine, Toronto, Section of Paediatrics

Chairman: Dr. Bernard Laski, Toronto.
Secretary: Dr. Crawford Anglin, Toronto.
Place: Academy of Medicine.

British Paediatric Association

President: Prof. J. Smellie.
Secretary: Prof. Alan Moncrieff, Institute of Child Health, The Hospital for Sick Children, Great Ormond St., W. C. 1, London.
Place: Windermere. Time: Between Easter and Whitsunday.

Canadian Paediatric Society

President: Dr. D. B. Leitch, 210 McLeod Bldg., Edmonton, Al.
Secretary: Dr. R. L. Denton, 1615 Cedar Ave., Montreal 25.

Danish Pediatric Society

President: Dr. A. Rothe-Meyer, Children's Hospital Fûglebakken, Copenhagen F.
Secretary: Dr. E. Winge Flensborg, Children's Hospital Mantinsvej, Copenhagen V.
Place: Different hospitals. Time: First Wednesday of every month.

Departmento de Pediatria da Associação Paulista de Medicina

President: Dr. Oswaldo Riedel de Souza e Silva.
Secretaries: Dr. Ovidio Collesi.
Dr. Helda Elina Vieira de Barros.
Place: Avenida Brigadeiro Luiz Antonio, 278, São Paulo, Brasil.

*Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Deutsche Gesellschaft für Kinderheilkunde

President: Prof. Dr. Adam, Universitats Kinderklinik, Erlangen.
Secretary: Prof. Dr. Jochims, Städtische Kinderklinik, Lübeck.
Place: Bayreuth. Time: Sept. 1-4, 1952.

Hellenic Society of Pediatrics

President: Dr. Spiros Charocopos, Alexandras Ave. 1, Athens.
Secretary: Dr. Nikas Zervos.
Place: Amphitheater, Medical School of the University of Athens. Time: Once a month.

Nederlandse Vereniging voor Kindergeneeskunde

President: Dr. G. J. Huët, 39 Brediusweg, Bussum.
Secretary: Dr. H. Reerink, % Sophia Kinderziekenhuis, 160 Gordelweg, Rotterdam.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

Norsk Pediatrisk Selskap

President: Dr. Arne Njå, Sporveisgt. 29, Oslo.
Secretary: Dr. Helge Granrud, Abbedikollen 38, Bestun, Oslo.
Place: Barneklinikken, Rikshospitalet, Oslo. Time: Friday, six times a year.

Philippine Pediatric Society

President: Dr. Renato Ma. Guerrero.
Secretary: Dr. Felix A. Estrada.
Place: Santo Tomas University Hospital and other pediatric centers. Time: Every two months.

Schweizerische Gesellschaft für Pädiatrie

President: P. D. Dr. F. Bamatter, St.-Léger 8, Genève.
Secretary: Dr. M. Nicod, Place Bel-Air 2, Lausanne.

Sociedad Argentinade Pediatrie

President: Dr. Rudolfo Kreutzer.
Secretary: Dr. Luis M. Cucullu.
Place: Sante Fè 1178, Buenos Aires.

Sociedad Chihuahuense de Pediatría

President: Dr. Alfonso Ruiz Escalona.
Secretary: Dr. Armando G. Herrera.
Place: Hospital Infantil del Estado, Chihuahua, Chih., México.

Sociedad Cubana De Pediatria

President: Prof. Agustin Castellanos y Gonzales.
Secretary: Dr. Carlos Hernandez Miyares, Apartado 2430, Habana.
Place: Catedra de Clinica Infantil Hospital Nuestra Senora de las Mercedes and Hospital Municipal de Infancia, Habana. Time: 9 p.m., last Wednesday of every month.

Sociedad de Pediatría de Concepción (Chile)

President: Dr. Jacinto Rojas.
Secretary: Dr. Guillermo Repetto D.
Place: Hospital Clinico Reginal Concepción. Time: 7:30 p.m., second Tuesday of every month, April to December, inclusive.

SOCIEDAD URUGUAYA DE PEDIATRIA

President: Dr. Euclides Peluffo.

Secretary: Dr. Ruben Gorlero Bacigalupi.

Place: Av. Agraciada 1464, piso 13, Montevideo.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRÍA

President: Dr. Guillermo Rangel.

Secretary: Dr. Guillermo Tovar E., P.O. Box 5, Caracas.

Place: Hospital Municipal de Niños, Caracas. Time: Once a month.

LA SOCIÉTÉ DE PÉDIATRIE DE MONTRÉAL

President: Dr. Henri Charbonneau, 3095 Sherbrooke, Montréal.

Secretary: Dr. Edmond Baril, 301 Carré St-Louis, Apt. 1, Montréal.

Time: Second Thursday of each month.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Prof. Jean Cathala, 45 rue Scheffer, Paris XVI.

Secretary: Prof. Maurice Lamy, 94 rue de Varenne, Paris VII.

Place: Hôpital des Enfants Malades, 149 rue de Sèvres, Paris XV. Time: 4 p.m., third Tuesday of each month.

SOCIÉTÉ DE PÉDIATRIE DE QUÉBEC

President: Dr. Roland Thibaudeau, 203 des Erables, Québec.

Secretary: Dr. Euclide Dechêne, 312 du Roi, Québec.

Place: Quebec. Time: May and November.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Docent Urban Hjarne, Stockholm.

Secretary: Dr. M. d'Avignon, Pediatric Clinic, Karolinska Sjukhuset, Stockholm 60.

Place: Swedish Medical Society, Klara Östra Kyrkogata 10, Stockholm, and Pediatric Clinic, Upsala. Time: Second Friday of each month, except summer.

UNITED STATES

National

AMERICAN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Walter B. Stewart, 8 N. Tallahassee Ave., Atlantic City, N. J.

Secretary: Dr. Wyman C. C. Cole, 3001 W. Grand Blvd., Detroit.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Warren W. Quillian, 140 Alhambra Circle, Coral Gables, Miami 34, Fla.

Secretary: Dr. E. H. Christopherson, 636 Church St., Evanston, Ill:

Place: Palmer House, Chicago. Time: Oct. 20-23, 1952.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Horace Hodes.

Secretary: Dr. Sydney S. Gellis.

THE AMERICAN PEDIATRIC SOCIETY

President: Dr. Hugh McCulloch, La Rabida Jackson Park Sanitarium, Chicago 49.

Secretary: Dr. Aims C. McGuinness, 237 Medical Laboratories, University of Pennsylvania, Philadelphia 4.

Sectional

Intermountain Pediatric Society

President: Dr. John T. Mason.

Secretary: Dr. Stanley R. Child.

Place: Ambassador Athletic Club, Salt Lake City. Time: 7 p.m.

New England Pediatric Society

President: Dr. Albert W. Fellows.

Secretary: Dr. Harry Shwachman, 300 Longwood Ave., Boston.

Place: Boston, except Spring meeting. Time: Wednesdays, four times a year.

North Pacific Pediatric Society

President: Dr. Carl Ashley, 2455 N. W. Marshall St., Portland, Ore.

Secretary-Treasurer: Dr. S. Gorham Babson, 1107 S. W. 13th St., Portland, Ore.

Place: Sun Valley, Idaho (1952), Seattle (1953). Time: September, 1952, and March, 1953.

Northwestern Pediatric Society

President: Dr. F. G. Hedenstrom, 420 Lowry Medical Arts Bldg., St. Paul.

Secretary: Dr. Charles L. Steinberg, 1118 Lowry Medical Arts Bldg., St. Paul.

Place: Minneapolis; St. Paul; Duluth, Minn., and Rochester, Minn. Time: January, April, July, and October.

Rocky Mountain Pediatric Society

President: Dr. John Lichty, Pediatric Department, Colorado General Hospital, 4200 E. 9th Ave., Denver.

Secretary: Dr. Edwin T. Williams, 1850 Gilpin St., Denver 6.

Place: Announced by mail. Time: Monthly dinner meetings, October to June.

Southwestern Pediatric Society

President: Dr. Clement J. Molony, 416 N. Bedford Dr., Beverly Hills, Calif.

Secretary: Dr. Carl A. Erickson, 960 E. Green St., Pasadena, Calif.

Place: Jonathan Club of Los Angeles. Time: 6:30 p.m., second Wednesday in January, March, May, September, and November.

State

Alabama Pediatric Society

President: Dr. David B. Monsky, 748 Adams St., Montgomery 5.

Secretary: Dr. Alice H. Pye, 305 Church St., Montgomery.

Place: Montgomery.

Arizona Pediatric Society

President: Dr. Henry E. Running.

Secretary: Dr. William F. Schaffman.

Time: On Call.

California Medical Association, Section on Pediatrics

Chairman: Dr. Joseph W. St. Geme, 511 S. Bonnie Brae, Los Angeles 5.

Secretary: Dr. Alvin H. Jacobs, 2201 Webster St., San Francisco 15.

Assistant Secretary: Dr. Clement J. Molony, 416 N. Bedford Dr., Beverly Hills.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Joseph Hetzel, 51 Central Ave., Waterbury.

Secretary: Dr. James H. Root Jr., 103 N. Main St., Waterbury.

Time: With the Connecticut State Medical Society in the spring, with the Connecticut State Clinical Congress in the fall; winter meeting usually in December.

Illinois State Medical Society, Section on Pediatrics

Chairman: Howard R. Miller, 418 Jefferson Bldg., Peoria 2.
Secretary: Harry H. Boyle, 2376 E. 71st St., Chicago 49.

Indiana State Pediatric Society

President: Dr. Harold D. Lynch, Evansville.
Secretary: Dr. L. T. Meiks, Indianapolis.

Iowa Pediatric Society

President: Dr. John McKitterick, 315 Tama Bldg., Burlington.
Secretary: Dr. James Dunn, 501 Davenport Bank Bldg., Davenport.

Massachusetts Hospital Association

President: Dr. Philip D. Bonnet, Administrator, Massachusetts Memorial Hospitals, Boston.
Executive Secretary: Henry G. Brickman, 14 Somerset St., Boston 8.
Place: Boston. Time: Annual Meeting, January, 1953.

Michigan State Medical Society, Pediatric Section

President: Dr. Horace L. French, 301 Seymour Ave., Lansing.
Secretary: Dr. Park S. Bradshaw, 1014 Jefferson St., Muskegon.
Place: Detroit: Time: September, 1952.

Montana Pediatric Society

President: Dr. Orville M. Moore, 555 Fuller Ave., Helena.
Secretary: Dr. Joseph W. Brinkley, 410 Central Ave., Great Falls.
Place: Variable. Time: Spring and fall.

Nebraska Pediatric Society

President: Dr. George J. Klok.
Secretary-Treasurer: Dr. Donald C. Nilsson, 115 N. 40th St., Omaha.
Place: Children's Memorial Hospital. Time: 6 p.m., dinner, third Thursday of each month from October to June, inclusive.

New Hampshire Pediatric Society

President: Dr. Douglass W. Walker, Laconia.
Secretary: Dr. Wm. D. Penhale, Concord.
Place. Alternately Concord, Hanover, Laconia, and Manchester. Time: Four times a year.

New Mexico Pediatrics Society

President: Dr. M. K. Wylder, Suite 14, Medical Arts Sq., Albuquerque.
Secretary: Dr. Ly Werner, Suite 25, Medical Arts Sq., Albuquerque.
Place: Variable. Time: Every two or three months.

South Carolina Pediatric Society

President: Dr. Walter Moore Hart, 117 W. Cheves St., Florence.
Secretary: Dr. John R. Paul Jr., 82 Rutledge Ave., Charleston.
Place: Columbia, S. C. Time: Second Monday and Tuesday in September; Sept. 8 and 9, 1952.

Tennessee Pediatric Society

President: Dr. O. L. Von Canon, 846 McCallie Ave., Chattanooga.
Secretary: Dr. Oliver W. Hill, 4807 Newcom Ave., Knoxville.

Texas Pediatric Society

President: Dr. C. S. E. Touzel, 1111 Pennsylvania Ave., Fort Worth.

Secretary: Dr. M. C. Carlisle, 1410 Austin Ave., Waco.

Treasurer: Dr. Edith Bonnet, 228 Medical Arts Bldg., San Antonio.

Place: Dallas. Time: Oct. 17 and 18, 1952.

Virginia Pediatric Society

President: Dr. Edwin L. Kendig Jr.

Secretary: Dr. T. J. Humphries.

Wisconsin State Medical Society

Chairman: Dr. Franklin J. Mellencamp, 1513 E. Capitol Dr., Milwaukee 11.

Secretary: Dr. E. H. Pawsat, 44 S. Marr St., Fond du Lac.

Local

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. C. T. J. Dodge, 15457 Euclid Ave., Cleveland 12.

Secretary: Dr. Beulah Wells, 10515 Carnegie Ave., Cleveland 6.

Place: Allen Memorial Medical Library. Time: 8:15 p.m., October, December. February, and March.

Baltimore City Medical Society, Pediatric Section

President: Dr. Wilson Grubb, 4 E. 33d St., Baltimore 18.

Secretary: Dr. Gibson J. Wells, 3101 St. Paul St., Baltimore 18.

Place: 1211 Cathedral St., Baltimore 1. Time: 8:30 p.m., second Tuesday in November, January, and March.

Brooklyn Academy of Pediatrics

President: Dr. Bernard Benjamin, 845 Park Pl., Brooklyn.

Secretary: Dr. Henry Cohen, 1761 E. 19th St., Brooklyn.

Place: Granada Hotel, Brooklyn. Time: 8:45 p.m., fourth Wednesday of February, March, April, October, and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold.

Secretary: Dr. Richard A. Downey.

Place: Children's Hospital, 219 Bryant St. Time: 8:30 p.m., first Monday of each month, September to June.

Central New York Pediatric Club

President: Dr. Frank Williams, 58 Swan St. S., Albany.

Secretary: Dr. Fred W. Bush, 325 Park Ave., Rochester.

Place: Various cities in New York State; fall meeting jointly with Upper New York State Academy of Pediatrics. Time: Third Tuesday of April and October.

Central Ohio Pediatric Society

President: Dr. E. V. Turner, 2479 E. Main St., Columbus.

Secretary: Dr. James Beasley, Lancaster.

Place: As announced. Time: Third Wednesday of September, November, January, March, and May.

Chicago Pediatric Society

President: Dr. Craig Butler, 715 Lake St., Oak Park, Ill.

Secretary: Dr. Alfred S. Traisman, 6354 Broadway, Chicago 40.

Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Cincinnati Pediatric Society

President: Dr. Nelson W. Ryan, 1743 Madison Rd., Cincinnati.

Secretary: Dr. Joseph E. Ghoury, 2546 Auburn Ave., Cincinnati.

Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dade County Pediatric Society

President: Dr. Lynn Whelchel, DuPont Bldg., Miami, Fla.

Secretary: Dr. Howard Engle, 311 Lincoln Rd., Miami Beach, Fla.

Dallas Pediatric Society

President: Dr. Floyd A. Norman, 4325 Cole Ave., Dallas.

Secretary-Treasurer: Dr. Charles L. Smith, 4207 Lemmon Ave., Dallas.

Place: Children's Hospital of Texas. Time: 6:30 p.m., first Thursday in each month.

Detroit Pediatric Society

President: Dr. Ruben Meyer, 938 Maccabees Bldg., Detroit.

Secretary: Dr. W. W. Zuelzer, Children's Hospital of Michigan, Detroit.

Place: Variable. Time: Five times a year.

Honolulu County Pediatric Society

President: Dr. Teruo Yoshina, 1221 Victoria St., Honolulu.

Corresponding Secretary and Treasurer: Dr. John H. Peyton, Kauikeolani Children's Hospital, Honolulu.

Honolulu Pediatric Society

President: Dr. Teruo Yoshina, 1221 Victoria St., Honolulu.

Recording Secretary: Dr. M. H. Hasegawa.

Corresponding Secretary: Dr. John Peyton, Kauikeolani Children's Hospital, Honolulu.

Place: At doctors' homes in rotation. Time: 6 p.m., third Thursday of each month.

Houston Pediatric Society

President: Dr. Emanuel B. Brandes, 3101 Fannin St., Houston.

Secretary: Dr. Robert D. Lomas, 5101 Fannin St., Houston.

Place: River Oaks Country Club. Time: 7:30 p.m., fourth Tuesday of each month.

Kansas City Southwest Pediatric Society

President: Dr. Frank Hogue, Plaza Medical Bldg., Kansas City, Mo.

Secretary: Dr. S. J. Kranson, Truman Rd. and Ash, Independence, Mo.

Place: University Club, Kansas City, Mo. Time: On call.

Long Beach Pediatric Society

President: Dr. Kenneth Berkaw, 211 Cherry Ave., Long Beach, Calif.

Secretary: Dr. C. W. Latshaw, 3821 Atlantic Ave., Long Beach, Calif.

Place: Victor Hugo Restaurant, 730 E. Broadway. Time: First Tuesday night of every month.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Sidney Rosin, 6230 Wilshire Blvd., Los Angeles.

Secretary: Dr. Arthur J. Holmes, 65 N. Madison Ave., Pasadena 1.

Place: Los Angeles County Medical Association Bldg., 1025 Wilshire Blvd., Los Angeles. Time: Second Thursday of alternate months beginning in September.

Medical Society of the County of Kings and Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Irving S. Pearlman, 7602 Bay Pkwy., Brooklyn.

Secretary: Dr. Irving Weinstock, 350 Ocean Ave., Brooklyn.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave., Brooklyn. Time: 8:45 p.m., fourth Monday of April, October, November, January, and March.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. George Maksim, 1418 Good Hope Rd. S. E., Washington 20.

Secretary: Dr. John E. Cassidy, 5402 Connecticut Ave. N.W., Washington.

Place: Medical Society Bldg., 1718 M St. N.W., Washington. Time: Spring and fall.

Memphis Pediatric Society

President: Dr. James G. Hughes, 20 S. Dunlap, Memphis.

Secretary: Dr. George S. Lovejoy, 609 N. Highland, Memphis.

Place: Rotated among four hospitals. Time: 7:30 p.m., second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. Franklin Mellencamp, 1513 E. Capitol Dr., Milwaukee.

Secretary: Dr. Karl Beck, 1411 Wauwatosa Ave., Milwaukee.

Place: Milwaukee University Club. Time: Second Wednesday of February, April, June, and October.

Mobile Pediatric Society

President: Dr. Daniel Sullivan, 1420 Government St., Mobile, Ala.

Secretary: Dr. Robert O. Harris III, 1514 Government St., Mobile, Ala.

Place: Admiral Semmes Hotel. Time: 7:30 p.m., fourth Thursday of September, November, January, March, and May.

Nashville Pediatric Society

President: Dr. Thomas Weaver, Bennie Dillon Bldg., Nashville, Tenn.

Secretary: Dr. Ethel Walker, 3415 West End Ave., Nashville, Tenn.

Place: Homes of members. Time: Third Thursday of every month.

New York Academy of Medicine, Section on Pediatrics

Chairman: Dr. Jerome L. Kohn, 50 W. 96th St., New York 25.

Secretary: Dr. Lawrence B. Slobody, 1 E. 105th St., New York 12.

Place: New York Academy of Medicine, 2 E. 103d St. Time: 8:30 p.m., second Thursday of each month, November to May, inclusive.

Northern California Pediatric Society

President: Dr. John A. Anderson, Stanford Hospital, 2351 Clay St., San Francisco 15.

Secretary: Dr. Edward Campion, 1018 E St., San Rafael.

Place: San Francisco. Time: Quarterly, as speakers are available.

Oklahoma City Pediatric Society

President: Dr. C. M. Bielstein, 301 N.W. 12th St., Oklahoma City.

Secretary: Dr. Louis Frank, 1200 N. Walker St., Oklahoma City.

Place: Oklahoma Club. Time: On call.

Philadelphia Pediatric Society

President: Dr. Irving J. Wolman, 1740 Bainbridge St., Philadelphia 46.

Secretary: Dr. F. H. Harvie, 133 S. 36th St., Philadelphia 4.

Place: College of Physicians, 19 S. 22d St. Time: 8:30 p.m., second Tuesday from October to May, inclusive.

Pittsburgh Pediatric Society

President: Dr. Christian John Stoecklein, 519 Medical Arts Bldg., Pittsburgh 13.

Secretary-Treasurer: Dr. James W. Stirling, 694 Lincoln Ave., Pittsburgh 2.

Place: Western State Psychiatric Institute and Clinic. Time: Second Friday in October, December, February, and April.

Queens Pediatric Society

President: Dr. Samuel Dillon, 119-20 Rockaway Beach Blvd., Rockaway Park, N. Y.

Secretary: Dr. Moe Goldstein, 111-32 76th Ave., Forest Hills, N. Y.

Place: Seminole Club, 112th St. and 70th Rd., Forest Hills, N. Y. Time: Second Tuesday in October, December, February, and April.

Richmond Pediatric Society

President: Dr. Hobart T. Dougan, 1832 Monument Ave., Richmond 20, Va.

Secretary: Dr. Robert A. Hoffman, 1001 W. Franklin St., Richmond 20, Va.

Place: Medical College Hospital. Time: 8 p.m., third Thursday of each month, except June, July, and August.

San Antonio Pediatric Society

President: Dr. Edith M. Bonnet, 228 Medical Arts Bldg., San Antonio 5.

Secretary: Dr. Virginia S. Stovall, 1116 S. Texas Bldg., San Antonio 5.

Time: 7:30 p. m., supper, first Tuesday of each month.

Seattle Pediatric Society

President: Dr. Norman Cline.

Secretary: Dr. John Sterner.

Place: College Club. Time: 6:30 p.m., fourth Friday of each month from September to June.

St. Louis Pediatric Society

President: Dr. Maurice J. Lonsway.

Secretary: Dr. John C. Herweg.

Place: Candlelight House, 7800 Clayton Rd. Time: 6:30 p.m., second Thursday of each month from October to May, inclusive.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Fred J. Chapin, 101 John St., Bay City.

Secretary-Treasurer: Dr. George H. Lowrey, University Hospital, Ann Arbor.

Place: University Hospital, Ann Arbor. Time: October, 1952.

Waco Pediatric Society

President: Dr. J. M. Garrett, 1408 Austin Ave., Waco, Texas.

Secretary: Dr. C. G. Shellenberger, 1318 Austin Ave., Waco, Texas.

Place: 1917 Austin Ave., Waco, Texas. Time: Third Tuesday of each month.

Westchester County Medical Society, Pediatric Section

President: Dr. Herbert Kahan, 650 Main St., New Rochelle, N. Y.

Secretary: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: The Roger Smith Hotel, White Plains, N. Y. Time: Four dinner meetings a year, November, February, April, and June.

Western Michigan Pediatric Society

President: Dr. A. Morgan Hill, 310 Fulton, E., Grand Rapids.

Secretary: Dr. John C. Montgomery, 1810 Wealthy St., S.E., Grand Rapids.

Place: Two meetings in Grand Rapids, two elsewhere. Time: First Wednesday of October, November, April, and May.

Wichita Pediatric Society

President: Dr. Vincent Scott, Schweiter Bldg., Wichita, Kan.

Secretary: Dr. William F. McGuire, 3241 E. Douglas, Wichita, Kan.

Place: Homes of members. Time: 8:30 p.m., first Thursday, October through May.

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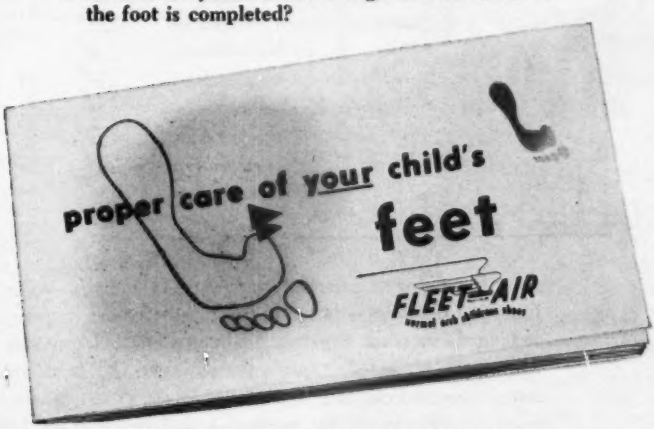

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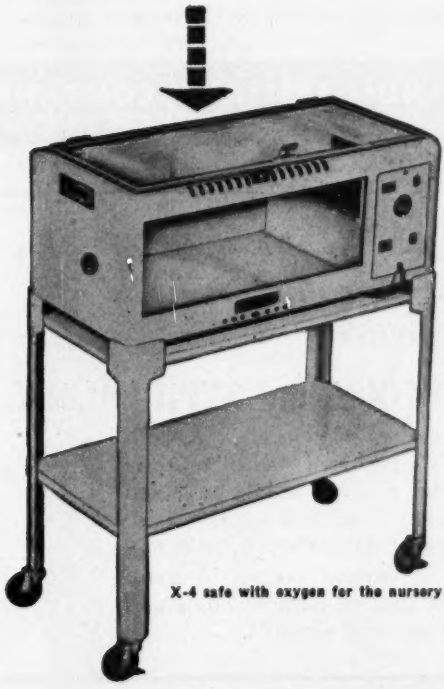

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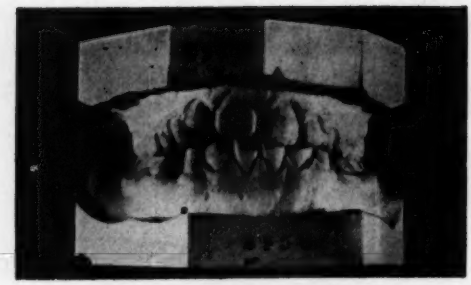

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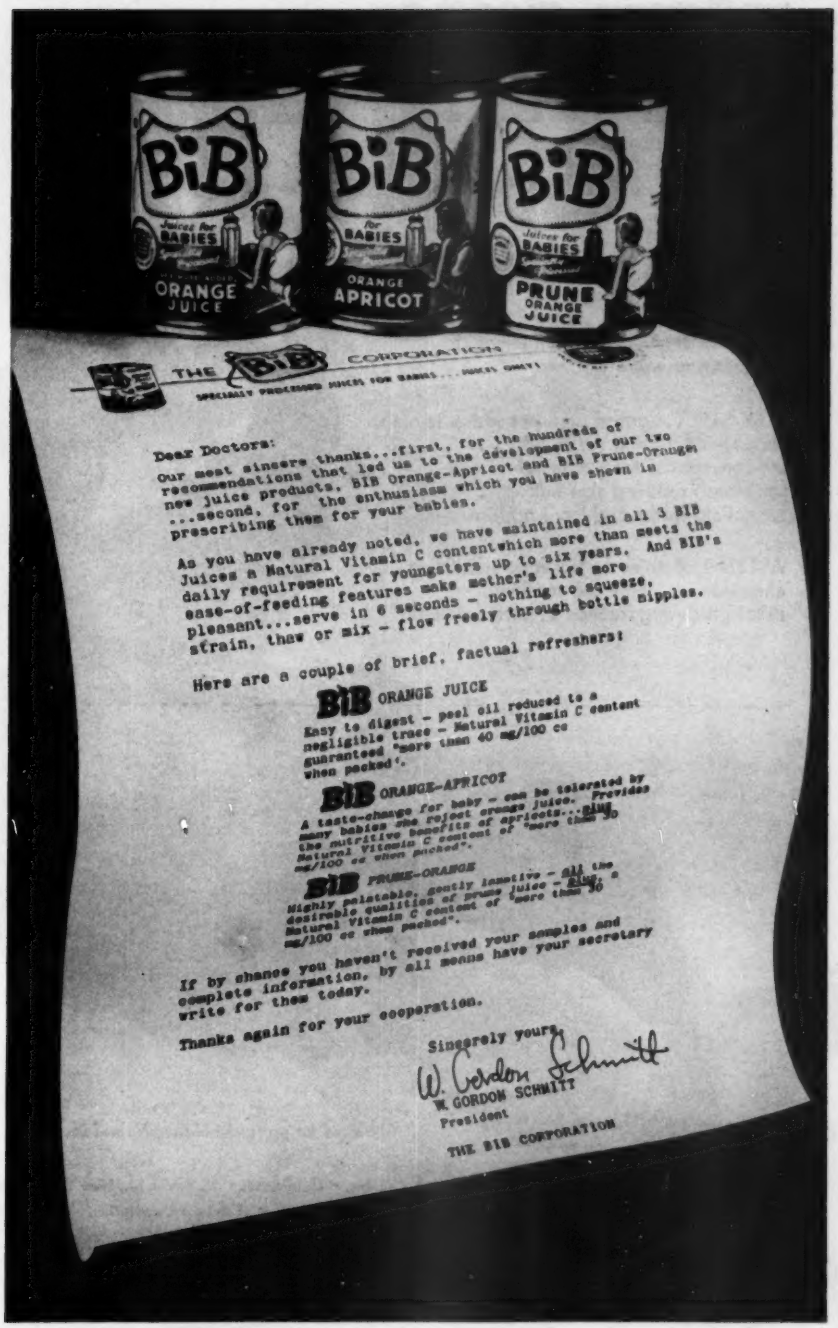
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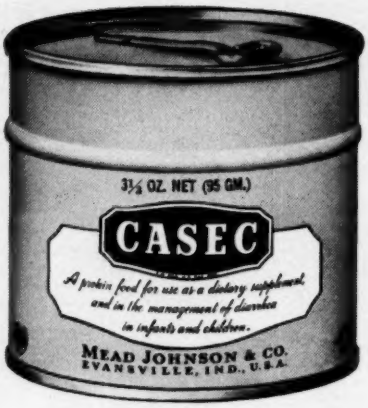
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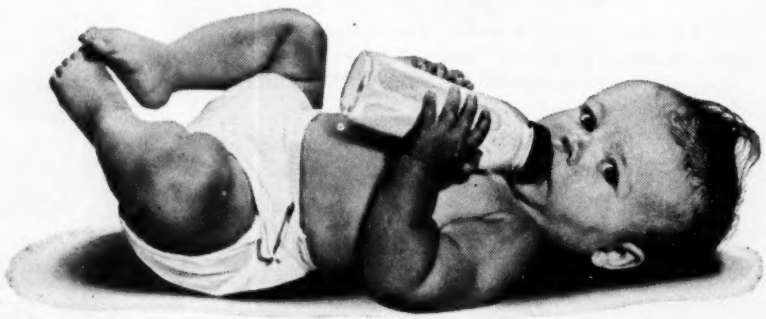

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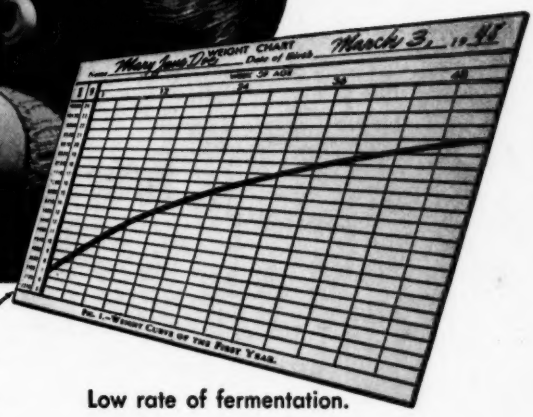

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